# Measurement Error in Designed Experiments for Second Order Models

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(ABSTRACT)

Measurement error (ME) in the factor levels of designed experiments is often overlooked in the planning and analysis of experimental designs. A familiar model for this type of ME, called the Berkson error model, is discussed at length. Previous research has examined the effect of Berkson error on two-level factorial and fractional factorial designs. This dissertation extends the examination to designs for second order models. The results are used to suggest optimal values for axial points in Central Composite Designs.

The proper analysis for experimental data including ME is outlined for first and second order models. A comparison of this analysis to a typical Ordinary Least Squares analysis is made for second order models. The comparison is used to quantify the difference in performance of the two methods, both of which yield unbiased coefficient estimates. Robustness to misspecification of the ME variance is also explored.

A solution for experimental planning is also suggested. A design optimality criterion, called the $D_{ME}$ criterion, is used to create a second-stage design when ME is present. The performance of the criterion is compared to a D-optimal design augmentation. A final comparison is made between methods accounting for ME and methods ignoring ME.

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# 1. Introduction

## 1.1 The Problem

The objective of this research is to explore measurement error in the design factors of designed experiments. The error occurs when a specified treatment level for a design factor differs from the treatment amount received by the experimental unit. Measurement error affects the choice of analysis of the experimental data. It can also affect the properties of the experimental design. This dissertation will address the problem of measurement error from both analysis and design perspectives.

Measurement error in designed experiments exists in many different industries and areas of research. One example is the field of toxicology. The methodology of some aquatic toxicology experiments involves applying mixtures of aromatic hydrocarbons to experimental units. The mixtures are applied directly to a laboratory environment such as a test tube or artificial stream. Achieving the desired level of chemical within a mixture can be practically impossible, since the hydrocarbons evaporate quickly in an open environment and are not easily captured within the atmospheres in which the aquatic organisms live. Another example is designed experiments for food manufacturing processes. In some situations, maintaining a desired temperature setting for an oven may be difficult or impossible. A third example is the application of a fertilizer or chemical to an agricultural plot. The fertilizer may not be spread evenly across the experimental unit, leading to observations of the response that are not equivalent to the response at the desired application level. In each of these situations, the measurement error is the result of failure to achieve desired design levels for the experimental unit. This error can lead to faulty conclusions in the analysis of the experimental results, since the researcher unknowingly bases inferences on the designed levels rather than the true levels achieved for each factor in the experiment.

Although it seems inappropriate to plan an experiment when measurement error is present in the design factors, there are cases where information is desired and control of the factor settings is impossible. This problem differs from Genichi Taguchi's "noise variable problem" [Taguchi & Wu (1980), Taguchi (1986, 1987)]. Noise variables can be controlled in a laboratory setting, so that the experimental levels of the factors are received by the experimental unit without error. However, to make use of the resulting optimal design factor levels is not possible. The factors are considered uncontrollable in large-scale manufacturing settings or other "real life" situations.

In a situation involving measurement error in the experimental design, the factors are never completely controllable. The same control over the factor level exists in both the experimental and large-scale manufacturing situations. However, there may be opportunities to explore the variability in the design factor. In each of the examples mentioned previously, post-experimental observations of the deviations in factor levels from the desired values may yield some idea of the inconsistencies between design values and true factor settings for the experiment. This information may be used to plan for future designs.

This research explores measurement error in designed experiments using several different approaches. Initially, the effect of measurement error on standard factorial designs is considered in relation to the design properties for first and second order models. This investigation reviews and extends the work of G.E.P. Box (1963) as discussed in later sections of the dissertation. Since accurate and precise information at each design point is especially critical in Response Surface designs such as the Central Composite Design (CCD) (Box & Wilson, 1951), Chapter 3 addresses the effect of measurement error on CCDs and attempts to find measurement error optimal CCDs for different situations. Chapter 4 outlines the correct analysis of experimental data involving measurement error and explores effects of measurement error in many different situations. Robustness issues concerning misspecification of measurement error magnitude are addressed in Chapter 5. Chapter 6 presents a design criterion for experimental data involving measurement error. Results are extended to two-factor designs in Chapters 7 and 8. Finally, the scope of future research in this area is summarized in Chapter 9.

## 1.2 Background

### 1.2.1 Errors-in-Variables Regression Models

The term *measurement error* (ME) refers to the inexact observation of some quantity which may be either constant or variable in nature. Although a main assumption of linear models and their corresponding regression analyses is that the independent variables are known constants, this assumption is often idealistic and even unattainable. Measurement error has been the subject of investigation since the late 19th century, when Adcock (1877, 1878) considered the least squares solution to

$$y = \beta_0 + \beta_1 x$$

when both $x$ and $y$ are subject to error. The scope of ME research includes variable relationships in which $x$ and $y$ are interchangeable for modeling purposes as well as situations in which a distinction is made between the dependent ($y$) and independent ($x$) variable. The proposed research will involve the latter type of relationship.

Several different ME classifications exist. Each type of ME has distinguishing characteristics, which can be illustrated by examples using the following simple linear regression model:

$$y_i = \beta_0 + \beta_1 x_i + e_i, \quad i = 1, 2, ..., n, \qquad (1.1)$$

$$x_i = X_i + u_i,$$

where $y_i$ is the observed response having mean $\beta_0 + \beta_1 x_i$,
$\beta_0$ and $\beta_1$ are unknown parameters,
$e_i$ is a $N(0, \sigma_0^2)$ random error in the response,
$X_i$ is the observed value of the independent variable,
$x_i$ is the true unobserved value of the independent variable, and
$u_i$ is a random error in the observed independent variable having mean 0 and variance $\sigma_u^2$.

The variable $X$ is sometimes called the *manifest* variable, while the value $x$ is referred to as the *latent* variable. As research in the field of measurement error evolved, three basic models arose which describe the error structure in the independent variable (Fuller, 1987). They are known as the *structural* model, the *functional* model, and the *Berkson error* model.

In a structural model, the $x_i$ are treated as random variables so that all observations have a common mean and a variance differing only through the measurement error, i.e., $E(x_i) = \mu$. In this model, the observed outcome of the independent variable is the difference between two random values, $x_i - u_i$.

When the $x_i$ are fixed unknown values (or are considered deterministic variables), the model is called a functional model. In this case the observed outcome is the difference between a fixed unknown value and a random value.

The third situation occurs when the $X_i$ are design levels known to the experimenter, and the $x_i$ may be either a fixed or random factor. Then the relationship between the unknown $x_i$ value and the random error element is a fixed difference, namely $X_i$. This type of measurement error was first considered by J. Berkson (1950) and has been appropriately named for him. Each of these situations will be motivated by an example and examined in the simple linear regression setting.

An example of structural ME is the measurement of nitrogen content in a random sample of agricultural plots being used for experimentation throughout Virginia. The actual content of nitrogen in a field would be considered a random variable. The measurement would also contain some error due to a lack of uniformity of nitrogen across the field. Thus $X_i$ is the observed amount of nitrogen in field $i$, $x_i$ is the random variable representing the true amount of nitrogen in field $i$, and $u_i$ is the random variable representing the ME incurred through the measuring device or location of measurement. If specific fields are selected for the experiments (rather than a random sample of fields), the true amount of nitrogen in the soil is a fixed unknown amount ($x_i$), and the randomness associated with the observations ($X_i$) is due entirely to the ME incurred ($u_i$). In this case a functional model is appropriate for the ME.

In contrast to the above models, Berkson error occurs in an experimental design situation. The error takes place when the experimenter assumes that the experimental unit receives the treatment level assigned to it in the experimental design. Suppose an experimenter wants to measure the effect of a fertilizer through a designed experiment. If the fertilizer is applied to a field, the amount required by the experiment is a fixed, known amount ($X_i$). The actual fertilizer amount that reaches the soil ($x_i$) is an unknown value, and the ME ($u_i$) is the random value of the difference between that true value and the stated setting. It is easy to see that $x_i$ and $u_i$ can no longer be considered independent when we look at the model. The difference in the two unknown values is equal to the fixed value of the design level ($X_i$).

In each of the previously described situations, the response (plant heights, leaf area, etc.) is a function of unknown factor levels. However, the difference between the first two models and the Berkson error model lies in the interpretation of the manifest variable. For the Berkson error model, there is no error in the observation of $X_i$. The value is a constant. The error occurs only within the observation of $y_i$ and the inferences about $y$ based on the incorrect value $X_i$. For the models where $X_i$ is observed, error occurs in the observations of $X_i$ as well as $y_i$ and subsequent inferences. Another way of looking at these differences is to consider the effect of repeating the experiment or observation many times. For the structural and functional models, the focus is on $E(X_i) = x_i$, the expected value of the observed independent variable. However, the focus for the Berkson error model is on $E(x_i)$, the expected value of the true unobserved treatment level, which is *known* to be $X_i$.

To understand how these three models differ from a mathematical standpoint, Berkson (1950) considered the Ordinary Least Squares (OLS) estimator for the slope in a simple linear regression setting where both variables are centered:

$$b_1 = [\Sigma\, X_i y_i\,]/[\Sigma\, X_i^2].$$

When the factor levels are observed, as in the functional or structural cases, we insert the true factor values in the estimator and see that

$$b_1 = [\Sigma\,(x_i - u_i)(y_i)]/[\Sigma\,(x_i - u_i)^2] \qquad (\ 1.2\ )$$

$$= [\Sigma x_i(\beta_1 x_i + e_i) - \Sigma u_i(\beta_1 x_i + e_i)]/[\Sigma\,(x_i - u_i)^2]$$

$$= [\Sigma\beta_1 x_i^2 + \Sigma x_i e_i - \Sigma\beta_1 x_i\, u_i - \Sigma u_i e_i)]/[\Sigma\,(x_i - u_i)^2],$$

$$\text{and } E\,[b_1] = E\,[(\beta_1\Sigma x_i^2)/(\Sigma x_i^2 - 2\Sigma x_i u_i + \Sigma u_i^2)]$$

$$= \beta_1 \cdot E[(\Sigma x_i^2)/(\Sigma x_i^2 - 2\Sigma x_i u_i + \Sigma u_i^2)] \;\neq\; \beta_1,$$

$$\text{since } E[(\Sigma x_i e_i - \Sigma\beta_1 x_i\, u_i - \Sigma u_i e_i)\,/(\Sigma\,(x_i + u_i)^2)] = 0 \text{ and } E[(\Sigma x_i^2)/(\Sigma x_i^2 - 2\Sigma x_i u_i + \Sigma u_i^2)] \neq 1.$$

As a result, $b_1$ is a biased estimator of the slope in these two situations. Notice also that the estimate of the slope is multiplicatively biased toward zero. In contrast, the Berkson error case in which the values of the factors are controlled does not have this problem. The ME (as well as random error) is manifested in the observations of the dependent variable alone. Accordingly the estimate of the slope is

$$b_1 = [\Sigma\, X_i y_i\,]/[\Sigma\, X_i^2] \qquad (\ 1.3\ )$$

$$= [\Sigma\, X_i\,(\beta_1 x_i + e_i)]/[\Sigma\, X_i^2]$$

$$= [\Sigma\, X_i(\beta_1(X_i + u_i) + e_i)]/[\Sigma\, X_i^2]$$

$$= [\beta_1(\Sigma X_i^2 + \Sigma X_i u_i) + \Sigma e_i]/[\Sigma X_i^2],$$

and since $E[\Sigma X_i u_i] = E[\Sigma e_i] = 0$,

$$E[b_1] = \beta_1 \cdot E[(\Sigma X_i^2)/ (\Sigma X_i^2)] = \beta_1.$$

Thus the OLS estimator of the regression coefficient is unbiased in the Berkson case. The result of unbiased coefficient estimates for Berkson errors extends to more complex models, as will be demonstrated in future sections of this dissertation.

### 1.2.2 Experimental Design

Designed experiments are used to estimate relationships among variables by controlling a certain group of the variables. Factorial designs are a straightforward method of achieving this result for several variables simultaneously. However, if specific relationships among the variables are known to be important, smaller and more efficient designs are capable of this estimation. Examples of these smaller designs include fractional factorial and incomplete block designs (Hinkelmann & Kempthorne, 1995). These designs are usually considered for categorical factors where main effects and interactions (both two-way and higher order) are the effects of interest.

However, for design variables with continuous factors, Response Surface Methodology (RSM) allows the experimenter to create model-specific designs which achieve desirable estimation and prediction properties. For instance, suppose an experimenter believes a model which is linear in the coefficients is correct for his or her situation. The experimenter desires information on linear and quadratic effects for all factors and interaction effects for all factor pairs. He or she would then choose a second order response surface model for the experiment. Early work on second order designs includes the previously mentioned CCDs (Box & Wilson, 1951) and Box-Behnken Designs (BBDs) (Box & Behnken, 1960).

Design properties are sometimes discussed in terms of the design moments (Myers & Montgomery, 1995). Moments of the design may be defined as follows for a k factor design:

$[i] = \frac{1}{n} \sum_{m=1}^{n} x_{im}$ are the first order moments for each factor i = 1, ..., k,

$[ij] = \frac{1}{n} \sum_{m=1}^{n} x_{im}x_{jm}$ are the odd second order moments for factors i, j = 1, ..., k, $i \neq j$,

$[ii] = \frac{1}{n} \sum_{m=1}^{n} x_{im}^2$ are the even second order moments, and

$[iij] = \frac{1}{n} \sum_{m=1}^{n} x_{im}^2x_{jm}$, $[ijl] = \frac{1}{n} \sum_{m=1}^{n} x_{im}x_{jm}x_{lm}$, and $[iii] = \frac{1}{n} \sum_{m=1}^{n} x_{im}^3$

are the third order moments for factors i, j, l = 1, ..., k, $i \neq j \neq l$.

The pattern continues for any moments ([iijj], [iiii], [ijlm], etc.) which are of interest. A moment is considered odd if any power associated with a variable is odd, so that [iijjl] is an odd moment and [iijj] is an even moment. Designs are created to achieve certain properties based on moment values. For instance, a rotatable design has the property of equivalent prediction variance on spheres centered at the design center. For a second order model which is linear in the model coefficients, the moment requirements for rotatability are: (1) all odd moments through order 4 are zero, and (2) [iiii]/[iijj] = 3 (Myers & Montgomery, 1995). Many design optimality criteria are based on the design moment matrix

$$M = n^{-1}(X'X),$$

where X is the n *x* p model matrix for the design, and (X'X) is a p *x* p matrix containing the moments outlined previously according to the specified model for the system. These design criteria will be discussed in future sections of the dissertation.

The CCD will be an important design for the present research, so familiarity with the properties of a CCD is important. The design may be broken down into three parts: (1) a two level factorial or suitable fractional factorial in the *k* factors, with factor levels centered and scaled to 1 and -1, (2) two runs for each factor known as axial point runs, and (3) a certain number of experimental runs at the design center known as center runs. Axial points are set at -*d* and *d* for the specified factor, while all other factors are run at the center of the design. These points are so named because they lie on the axes of each design factor if the design is plotted. Examples of two-factor CCDs are shown in Table 1.1 and Figure 1.1.

Table 1.1 Two-Factor Central Composite Design with $d = 2$

| Run | $x_1$ | $x_2$ | type of point |
|---|---|---|---|
| 1 | -1 | -1 | factorial |
| 2 | -1 | 1 | " |
| 3 | 1 | -1 | " |
| 4 | 1 | 1 | " |
| 5 | -2 | 0 | axial |
| 6 | 2 | 0 | " |
| 7 | 0 | -2 | " |
| 8 | 0 | 2 | " |
| 9 - n | 0 | 0 | center |

The flexibility of a CCD lies in the choice of $d$ (almost always 1 or greater) for the axial points and in the number of center runs ($n_c$) used. Different properties can be achieved with these choices. The axial points give information about the quadratic effect for each factor, as do the center runs. The repetition of points in the center of the design also gives information about pure error. The factorial portion of the design gives information about main effects and interactions. Any design which allows all main effects and two factor interactions to be estimated is said to have resolution V or higher. Thus an appropriate fractional factorial for a CCD will be of resolution V or higher.

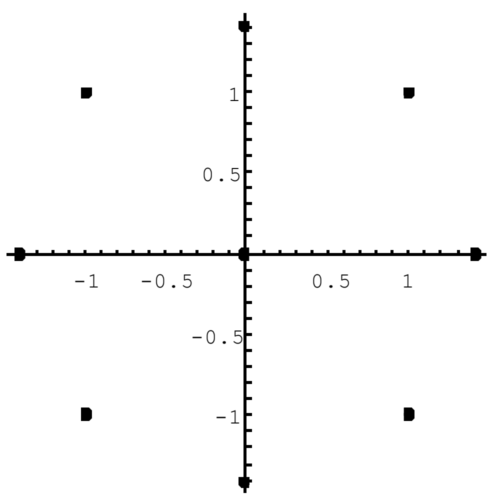


Figure 1.1 Two-Factor Central Composite Design with $d = \sqrt{2}$ and $n_c = 1$

### 1.2.2.1 Centering and Scaling

Whenever Response Surface methods are employed in an experimental design situation, the design levels are almost always specified in standardized units. For this reason, it is important to understand the effects of centering and scaling on the design factor levels. In later sections of the dissertation, the effect of design in the presence of ME will be clarified. However, the feasibility of using designs based on coded design variables must be established first. Since the designs in this dissertation involve only first and second order models, a second order model will be considered.

A second order model involving Berkson error in all k variables can be written as follows:

$$y_i = \beta_0 + \sum_{j=1}^{k} \beta_j (X_{ji} + u_{ji}) + \sum_{j=1}^{k-1} \sum_{m>j}^{k} \beta_{jm}(X_{ji} + u_{ji})(X_{mi} + u_{mi}) + \sum_{j=1}^{k} \beta_{jj}(X_{ji} + u_{ji})^2 + e_i \,. \quad (1.4)$$

The model can be rewritten to represent centered and scaled design variables with a new parameter vector $\underline{\gamma}$ as follows:

$$y_i = \gamma_0 + \sum_{j=1}^{k} \gamma_j \left( \frac{X_{ji} + u_{ji} - c_j}{d_j} \right) + \sum_{j=1}^{k-1} \sum_{m>j}^{k} \gamma_{jm} \left( \frac{X_{ji} + u_{ji} - c_j}{d_j} \right) \left( \frac{X_{mi} + u_{mi} - c_m}{d_m} \right)$$
$$+ \sum_{j=1}^{k} \gamma_{jj} \left( \frac{X_{mi} + u_{mi} - c_m}{d_m} \right)^2 + e_i.$$

Expansion of the individual terms in the model reveals that

$$\beta_{jj} = \gamma_{jj}/d_j^{\,2},$$
$$\beta_{jm} = \gamma_{jm}/(d_j \cdot d_m),$$
$$\beta_j = \gamma_j/d_j - (\gamma_{jm}/(d_j \cdot d_m))c_m - (2\cdot\gamma_{jj}/d_j^{\,2})c_j,$$
$$\text{and } \beta_0 = \gamma_0 - \sum_{j=1}^{k} (\gamma_j/d_j)c_j + \sum_{j=1}^{k-1} \sum_{m>j}^{k} (\gamma_{jm}/(d_j \cdot d_m))c_j c_m + \sum_{j=1}^{k} (\gamma_{jj}/d_j^{\,2})c_j^{\,2}.$$

Thus the coefficients from analysis of the original data are a simple linear transformation of the coefficients from an analysis of the centered and scaled design factor levels. The coefficient estimates may be calculated using either the original or centered and scaled data for X, and a simple transformation will yield results in the desired scale. The same transformation can be used to obtain variance estimates for the coefficients.

## 1.3 Related Research

Several statisticians have considered the ideas of ME in designed experiments as defined by Berkson. G.E.P. Box (1963) first explored factorial and fractional factorial designs in the presence of ME. Since 1963, the topics of Berkson error and its effect on experimental design have appeared infrequently throughout the literature. However, there are two papers after Box's article which consider design criteria in the presence of ME (Draper and Beggs, 1971; Vuchov and Boyadjieva, 1983). The conclusions of these authors are discussed below.

Box (1963) examined the consequences of ME in relation to experimental design by considering factorial and fractional factorial designs. He describes the true relationship between $y$ and $\underline{x}$ as

$$y_{\mathrm{i}} = g_d(x_{1\mathrm{i}}, x_{2\mathrm{i}}, \dots , x_{\mathrm{Ni}}) = g_d(X_{1\mathrm{i}} + u_{1\mathrm{i}}, X_{2\mathrm{i}} + u_{2\mathrm{i}}, \dots , X_{\mathrm{Ni}} + u_{\mathrm{Ni}}), \qquad (1.5)$$

$$\text{with } Y_{\mathrm{i}} = y_{\mathrm{i}} + e_{\mathrm{i}},$$

$$\mathrm{E}(u_{\mathrm{ji}}^2) = \sigma_{\mathrm{j}}^2,\ \ \mathrm{j} = 1, 2, \dots , \mathrm{N}, \text{ and } \mathrm{i} = 1, 2, \dots, \mathrm{n},$$
$$\mathrm{E}(u_{\mathrm{ji}}, u_{\mathrm{mi}}) = \rho_{\mathrm{jm}}\sigma_{\mathrm{j}}\sigma_{\mathrm{m}},\ \ \mathrm{j, m} = 1, 2, \dots , \mathrm{N},$$
$$\mathrm{E}(e_{\mathrm{i}}^2) = \sigma_0^2,\ \ \mathrm{i} = 1, 2, \dots , \mathrm{n},$$

where N is the total number of factors, and n is the number of observations of the response. In this study Box assumes there are k experimental factors, M factors held constant across all observations, and (N - k - M) "unrecognized" factors. The factors of relevance are the k experimental factors being varied across the experimental design. The function $g_d(\underline{x}_{\mathrm{i}}')$ is some polynomial function of degree $d$ in the $\underline{x}$'s. The observations are independent from response to response.

Box investigates the effect of ME for the first and second order model in detail. He finds (as does Berkson) that predicted values of the response based on a linear model are unaffected except for an increase in the variance of y, $\mathrm{var}(y_i) = \sigma_0^2 + \sum_{j=1}^{k} \beta_j^2\sigma_j^2$. As for the quadratic model, measurement error introduces a bias term in the predicted values of $y_i$. For instance, in a two factor quadratic model,

$$y_i = \beta_0 + \beta_1 x_{1i} + \beta_2 x_{2i} + \beta_{12}\, x_{1i}\, x_{2i} + \beta_{11} x_{1i}^2 + \beta_{22} x_{2i}^2 + e_i \qquad (1.6)$$

$$\begin{aligned} &= \beta_0 + \beta_1(X_{1i} + u_{1i}) + \beta_2(X_{2i} + u_{2i}) + \beta_{12}(X_{1i} + u_{1i})(X_{2i} + u_{2i}) \\ &\quad + \beta_{11}(X_{1i} + u_{1i})^2 + \beta_{22}(X_{2i} + u_{2i})^2 + e_i \end{aligned}$$

$$= \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \beta_{12} X_{1i} X_{2i} + \beta_{11} X_{1i}^2 + \beta_{22} X_{2i}^2 + \mathbf{B} + \varepsilon_i,$$

$$\text{where } \mathbf{B} = \beta_{12}\rho_{12}\sigma_1\sigma_2 + \beta_{11}\sigma_1^2 + \beta_{22}\sigma_2^2 \qquad (1.7)$$

is the bias associated with the measurement error in the factors, and

$$\begin{aligned} \varepsilon_i &= e_i + \beta_1 u_{1i} + 2\beta_{11} X_{1i} u_{1i} + \beta_{12} X_{2i} u_{1i} + \beta_2 u_{2i} + \beta_{12} X_{1i} u_{2i} \qquad (1.8) + \\ &\quad 2\beta_{22} X_{2i} u_{2i} + \beta_{12}(u_{1i} u_{2i} - \rho_{12}\sigma_1\sigma_2) + \beta_{11}(u_{1i}^2 - \sigma_1^2) + \beta_{22}(u_{2i}^2 - \sigma_2^2) \end{aligned}$$

$$\begin{aligned} &= e_i + \beta_1 u_{1i} + 2\beta_{11} X_{1i} u_{1i} + \beta_{12} X_{2i} u_{1i} + \beta_2 u_{2i} + \beta_{12} X_{1i} u_{2i} \\ &\quad + 2\beta_{22} X_{2i} u_{2i} + \beta_{12} u_{1i} u_{2i} + \beta_{11} u_{1i}^2 + \beta_{22} u_{2i}^2 - \mathbf{B}. \end{aligned}$$

is the variability due to measurement error in the factors and overall variability in the y values. Thus

$$E(y_i) = \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \beta_{12} X_{1i} X_{2i} + \beta_{11} X_{1i}^2 + \beta_{22} X_{2i}^2 + \mathbf{B}, \qquad (1.9)$$

$$E(\varepsilon_i) = 0,$$

$$\begin{aligned} \text{and } \mathrm{Var}(\varepsilon_i) &= \sigma_0^2 + \sigma_1^2[\beta_1 + \beta_{12} X_{2i} + 2\beta_{11} X_{1i}]^2 + \sigma_2^2[\beta_2 + \beta_{12} X_{1i} + 2\beta_{22} X_{2i}]^2 \\ &\quad + 2\rho_{12}\sigma_1\sigma_2[\beta_1\beta_2 + \beta_1\beta_{12} X_{1i} + 2\beta_1\beta_{22} X_{2i} + \beta_2\beta_{12} X_{2i} + \beta_{12}^2 X_{1i} X_{2i} \qquad (1.10) \\ &\quad + 2\beta_{12}\beta_{22} X_{2i}^2 + 2\beta_2\beta_{11} X_{1i} + 2\beta_{11}\beta_{12} X_{1i}^2 + 4\beta_{11}\beta_{22} X_{1i} X_{2i}] + K, \end{aligned}$$

where K is a constant including the higher order moments of $u_1$ and $u_2$. For this case as well as for quadratic models involving k > 2 factors, the variance of predicted values involves design levels.

Box justifies the use of factorial and certain fractional factorial designs in the presence of measurement error. He shows that any model effect coefficient estimate, such as $b_{11}$, has the property of unbiasedness. This is demonstrated for first and second order models by considering the properties of orthogonal, single degree of freedom contrasts which represent these effects. Note that the bias in $E[y_i]$ is constant for a second order model, so that $E(y_i(\underline{x})) = E(y_i(\underline{X})) + B$. Because contrasts are weighted sums of the $E[y_i]$ and are constructed so that the sum of the coefficients is zero,

$$E\left[\sum_{i=1}^{n} \alpha_i y_i(\underline{x})\right] = \sum_{i=1}^{n} \alpha_i E[y_i(\underline{X})] + B\cdot \sum_{i=1}^{n} \alpha_i = \sum_{i=1}^{n} \alpha_i E[y_i(\underline{X})] \qquad (1.11)$$

and any contrast would yield an unbiased estimate.

Box considers the effect of measurement error on the variance estimates for these model effects by defining single degree of freedom "residual" effect contrasts which combine to estimate the overall unexplained variation in $y$. The analysis of factorial designs can be completely defined using (n-1) contrasts for an n point design. Box uses this idea and presents certain requirements necessary for unbiased variance estimates. These requirements will be stated specifically in Chapter 2. They are shown to hold for all two level factorial designs. A fraction of a two level factorial with resolution $2d + 1$ will permit estimation of all effects in a polynomial of degree $d$ without bias in either coefficient estimates or variance of coefficient estimates. Blocking of designs can also be accomplished without complicating the estimates as long as the same odd design moments are nonzero within each block. This can be accomplished by creating the resolution in the same way in each block. Unequal replication of blocks is possible as well, if the "block design" is of resolution 3, i.e., the block types (based on signs associated with the different estimable effects) are not confounded with each other.

Box only explores the two level factorial designs and does not investigate designs capable of estimating a second order model. Response surface methodology often focuses on designs for second order models such as the CCD, since the factorial or fractional factorial design is universally accepted as optimal for the first order model. Further investigation into the problems associated with a second order model will be discussed in Chapter 2.

One nice contribution from Box is a general expression for the bias and variance of $y_i$ in the presence of ME when the true model is a polynomial of order $d$ in the $x_j$'s. The model is as follows:

$$y_i = g_d(\underline{x}_i) + e_i = g_d(\underline{X}_i) + B_i + \varepsilon_i,$$

where $B_i = E[g_d(\underline{x}_i)] - g_d(\underline{X}_i)$ and $\varepsilon_i = g_d(\underline{x}_i) - E[g_d(\underline{x}_i)] + e_i$.

Using a Taylor Series expansion,

$$B_i = \frac{1}{2!}\sum_{f1}\sum_{f2} E(u_{f1i}u_{f2i}) * \{\partial^2 g_d(\underline{X}) / \partial X_{f1}\partial X_{f2}\} \quad + \ldots$$
$$+ \frac{1}{d!}\sum_{f1}\sum_{f2}\cdots\sum_{fd} E(u_{f1i}u_{f2i}\ldots u_{fdi})\cdot\{\partial^d g_d(\underline{X}) / \partial X_{f1}\partial X_{f2}\ldots\partial X_{fd}\},$$

(1.12)

$$\varepsilon_i = \sum_{f1} u_{f1i} - E(u_{f1i})\cdot\{\partial g_d(\underline{X}) / \partial \mathbf{X}_{f1}\} \quad + \ldots$$
$$+ \frac{1}{d!}\sum_{f1}\sum_{f2}\cdots\sum_{fd} u_{f1i}u_{f2i}\ldots u_{fdi} - E(u_{f1i}u_{f2i}\ldots u_{fdi})\cdot\{\partial^d g_d(\underline{X}) / \partial X_{f1}\partial X_{f2}\ldots\partial X_{fd}\} + \mathbf{e_i}.$$

where $f1, f2, \ldots, fd = 1, 2, \ldots,$ N are the placeholders for each factor contained in the polynomial term. The expressions allow the researcher to explore new techniques for minimizing $B_i$ and $E(\varepsilon_i^2)$, two main concerns of response surface designs. Box concludes that bias($y_i$) = $B_i$ is a function of degree $d$ - 2 in the k experimental factors and var($y_i$) = $E(\varepsilon_i^2)$ is a function of degree 2$d$ - 2 in the experimental factors. Thus the bias in predicted values from models with cubic or higher order non-interaction terms is dependent upon the design, and variance of quadratic and higher models is affected by design.

Several years after Box's work on factorial designs, Draper and Beggs (1971) considered a design criterion based on

$$w_i = \hat{y}_X(X_i) - \hat{y}_x(X_i) = \underline{X}_i'[(X'X)^{-1}X' - (Z'Z)^{-1}Z']y, \qquad (1.13)$$

which is the difference between prediction based on the designed levels and prediction based on the actual levels (denoted by $Z$) at a point in the original design. The criterion minimizes the quantity

$$G = E_{error}E_{y|error}[\Sigma_i\, w_i^2],$$

which can be interpreted as an overall measure of expected discrepancy between the two surfaces in terms of prediction at design points. Relying on the assumptions that third and higher order powers in the errors may be ignored and that a matrix involving factor by factor error interactions converges to the null matrix, G is shown to be approximated by

$$G \cong \underline{\beta}'E_{error}[(Z - X)'X(X'X)^{-1}X'(Z - X)]\underline{\beta} + \sigma_0^2\, \mathrm{tr}\,(M^{-1}\cdot n^{-1}E_{error}[(Z - X)'(Z - X)]), \quad (1.14)$$

where M is the design moment matrix. The criterion is applied to a first order model with several different cases: uncorrelated factor errors, all factor error correlations equal, and for two special groupings of factor error correlations. The resulting designs are reported in terms of design moment requirements. For uncorrelated errors, the typical design with all odd moments at zero is reported. This design agrees with optimal first order designs in a linear model ignoring ME. For all other correlation structures, the first order moments are zero and the odd second order moments are a function of the correlation between factors, the variance of the individual factors, and the chosen value for the even second order design moments. These values increasingly differ from zero as the correlation between factors increases.

It should be noted that the designs given by Draper and Beggs will be robust for prediction when ME is present, but the overall prediction performance of the designs is not discussed. Thus a design may work very well at eliminating misleading information, but the quality of the information (variance of coefficients, prediction variance, etc.) may suffer.

A few years later, Vuchov and Boyadjieva (1983) developed two new criteria for evaluating designs based on linear models in the presence of factor errors. Their work considers a model

$$\underline{y} = F\underline{\beta} + \underline{\varepsilon}^*, \qquad (1.15)$$

where G = $Z$ - $X$, the difference between the true and the designed model matrix,

$$F = X + E_u[G],$$

$$\text{and } \underline{\varepsilon}^* = \underline{e} + (G - E_u[G])'\underline{\beta}.$$

Assuming the $e_i$ and the $\underline{u}_i$ (the variations from the designed values) are independent,

$$\text{var}(\varepsilon^*_i) = \underline{\beta}'A_i\underline{\beta} + \sigma_0^2,\ i=1, 2, \ldots, n, \qquad (1.16)$$

where $A_i = E_u[(\underline{g}_i - E_u[\underline{g}_i])(\underline{g}_i - E_u[\underline{g}_i])']$.

If the design is for a first order model, then OLS yields the best linear unbiased estimates for the coefficients. If, however, the design is not linear in the factors, the following weighted least squares estimates would be best:

$$\underline{b} = (F'W^{-1}F)^{-1}F'W^{-1}\underline{y},$$

where W = diag($\varepsilon^*_i$) . Supposing that the OLS estimates are used when measurement error in the factors is present, a design robust to these weights would have very similar values of $\varepsilon^*_i$ for all i.

The first criterion minimizes the heteroscedasticity of variance within the design employed, by minimizing the maximum $\text{var}(\varepsilon^*_i)$ across the design. In most common cases this criterion is equivalent to

$$\text{Minimize}_{(\text{design})} : n^{-1}\max_{(i)} (\lambda_i - 1),$$

where $\lambda_i$ is the maximum root of $\det|A_i - \lambda A^*| = 0$ and $A^* = \text{ave}_{(i)}\ A_i = n^{-1}\sum A_i$. As in the case of the criterion proposed by Draper and Beggs, this method will produce a design which is robust to measurement error but may or may not have other desirable design properties.

The second criterion is concerned with minimizing the trace of the covariance matrix of $\underline{\beta}$. Since

$$V(\underline{\beta}) = (F'F)^{-1}F'WF(F'F)^{-1},$$

the trace of the covariance matrix of $\underline{\beta}$ can be written as

$$\text{tr}(V(\underline{\beta})) = \text{tr}(WF(F'F)^{-2}F') = \text{tr}(WS),$$

where $S = F(F'F)^{-2}F'$. The authors provide a theorem which allows the traces from two designs to be compared according to the quantity

$$\underline{\beta}'\Delta R\underline{\beta} + \sigma_0^2\Delta r,$$

where $\Delta R = (\Sigma A_i s_i)_{\text{design2}} - (\Sigma A_i s_i)_{\text{design1}}$,
$\Delta r = (\Sigma s_i)_{\text{design2}} - (\Sigma s_i)_{\text{design1}}$, and
$s_i$ is the i-th diagonal of the matrix S. If this quantity has positive value then design 1 has a smaller trace than design 2 and is a better design in the presence of factor errors. Since the criterion requires knowledge of the model coefficients, there are several limitations to design comparisons. If $\Delta R$ is a positive definite matrix and $\Delta r$ is a positive quantity, then design 1 is better than design 2 for any set of coefficients $\underline{\beta}$. If $\Delta R$ is positive definite and $\Delta r$ is a negative quantity, then design 1 is better than design two for certain $\underline{\beta}$ vectors outside of an ellipsoid based on the values of $\sigma_0^2$, $\Delta r$, and the eigenvalues of $\Delta R$. If $\Delta R$ is not positive definite, then the designs are incomparable by this criterion.

Vuchov and Boyadjieva concluded their research by comparing several well-known designs based on the two developed criteria. In many cases, the two criteria chose different designs. This is probably a result of the different goals of the two criteria. The first criterion attempts to minimize the effect of the ME, while the second criterion attempts to estimate the model coefficients efficiently in the presence of ME.

Other areas of research incorporating the Berkson error model are coefficient estimation for binary regression models (Burr, 1988) and Bayesian analysis of nonlinear regression models (Dellaportas and Stephens, 1995). Both papers focus on the analysis of regression models with Berkson error rather than design of the controlled experiments, so these papers will not be described further.

# 2. ME and Variance Estimates in the Second Order Model

Box (1963) described the analysis of n-point factorial designs by creating n-1 single-degree orthogonal contrasts. These contrasts represent both effects of interest in the model and effects not appearing in the model. There are p-1 contrasts representing effects in a model containing p coefficients, since the intercept is not considered here. The remaining n-p non-model contrasts combine to form $s_r^2$, the estimated residual variance of the response variable. This overall variance estimate is used in the variance estimate for each model effect. Certain relationships within the set of contrasts must occur in order to achieve an unbiased estimate of the model effect variance from OLS analysis. These relationships, as stated below, are shown by Box to hold for all two level factorial designs as well as certain fractional factorial designs. It has been noted previously that the OLS analysis of data from models containing only linear, quadratic and interaction effects yields unbiased model effect estimates. However, the usual model effect variance estimates are biased for a second order model. This will be shown in the following sections. Section 2.1 will introduce the idea of residual variance as a function of residual contrasts. The next section will look at this residual variance for $3^k$ factorials. The effect of ME on the residual variance will be outlined in Section 2.3, and this effect will be demonstrated by two examples in subsequent sections of the chapter.

## 2.1 The Residual Variance

Consider a second order response surface model with k factors as follows:

$$y_i = \beta_0 + \sum_{j=1}^{k} \beta_j x_{ji} + \sum_{j=1}^{k-1} \sum_{m>j}^{k} \beta_{jm} x_{ji} x_{mi} + \sum_{j=1}^{k} \beta_{jj} x_{ji}^2 + e_i \, ,$$

where $e_i \sim N(0, \sigma_0^2)$. Notice that the response surface is a function of the true underlying values of the design variables. We can write each model effect as a contrast

$$\Lambda = \sum_{i=1}^{n} \alpha_i^* E[y_i],$$

which, in the presence of measurement error, has the unbiased estimate

$$L = \sum_{i=1}^{n} \alpha_i^* y_i$$

for first and second order models (Box, 1963) when $\Sigma\, \alpha_i^* = 0$. Note that a model effect contrast is signified by the coefficient $\alpha_i^*$, which will be important in distinguishing model effect coefficients from residual contrast coefficients. Residual contrast coefficients will be denoted by the coefficient $\alpha_g$. The variance for each contrast (in the absence of ME) is estimated by

$$\hat{\text{Var}}(L) = s_r^2\, \Sigma\, \alpha_i^{*2},$$

where $s_r^2$ is the estimated residual variance.

Recall that the entire set of n data points can be decomposed into n-1 single degree of freedom contrasts. All contrasts which represent effects which are not included in the model are *assumed* to have an expected value of 0 and a variance of $\sigma_0^2$, the variance of *y*. For this reason, $s_r^2$ may be written as the average of squared contrasts representing effects not included in the model. As previously noted, the coefficients of these contrasts will be denoted $\underline{\alpha}_g$, g = 1,2, ..., r = n - p, so that

$$s_r^2 = 1/r\ \left[ \sum_{g=1}^{r} \left( \sum_{i=1}^{n} \alpha_{gi} y_i \right)^2 \right].$$

In the absence of ME, Box indicated that the following properties must hold for these residual contrasts:

$$E[\sum_{i=1}^{n} \alpha_{gi} y_i] = 0,\ E[(\sum_{i=1}^{n} \alpha_{gi} y_i)^2] = \sigma_0^2, \text{ and } E[\sum_{i=1}^{n} \alpha_{gi} y_i \sum_{i=1}^{n} \alpha_{g'i} y_i] = 0,$$

$$g = 1, 2, ..., r, \text{ and } g \neq g'.$$

These properties will hold when the following statements are true for each of the *r* contrasts:

( 2.1 ) $\sum_{i=1}^{n} \alpha_{gi} E[y_i] = 0,$

( 2.2 ) $\sum_{i=1}^{n} \alpha_{gi}^2 = 1,$ and

( 2.3 ) $\sum_{i=1}^{n} \alpha_{gi}\alpha_{g'i} = 0, \forall g \neq g'.$

Since property ( 2.1 ) must hold for all possible sets of coefficient values in $E[y_i] = \underline{X}_i'\underline{\beta}$, it is equivalent to the following :

( 2.4 ) $\sum_{i=1}^{n} \alpha_{gi} = 0,$

( 2.5 ) $\sum_{i=1}^{n} \alpha_{gi} X_{ji} = 0, \forall j,$

( 2.6 ) $\sum_{i=1}^{n} \alpha_{gi} X_{ji} X_{mi} = 0, \forall j \neq m,$ and

( 2.7 ) $\sum_{i=1}^{n} \alpha_{gi} X_{ji}^2 = 0, \forall j.$

These properties hold for a $3^k$ unreplicated factorial design, as will be shown in the following section.

## 2.2 The Residual Variance for a $3^k$ Unreplicated Factorial Design

A quadratic model requires a three level design for estimation of the model coefficients, so the design discussed here is an unreplicated $3^k$ factorial with design levels at -1, 0, and 1. Because the design is unreplicated, all information about the variance of the responses is contained in $s_r^2$, the estimated residual variance. No estimate of pure variance is available. Each model effect is represented by a contrast $\Lambda$, and the coefficients for these contrasts are $\alpha_i^*(\beta)$. For any $3^k$ factorial the model effects may be calculated using the following sets of contrast coefficients:

(1) for linear effects,

$(\alpha_i^*(\beta_j) \mid X_{ji} = -1) = -(2\sum 3^{k-1})^{-1/2}$,
$(\alpha_i^*(\beta_j) \mid X_{ji} = 0) = 0$, and
$(\alpha_i^*(\beta_j) \mid X_{ji} = 1) = (2\sum 3^{k-1})^{-1/2}$,

(2) for quadratic effects,

$(\alpha_i^*(\beta_{jj}) \mid X_{ji}^2 = 1) = (2\sum 3^k)^{-1/2}$, and
$(\alpha_i^*(\beta_{jj}) \mid X_{ji}^2 = 0) = -2\sum(2\sum 3^k)^{-1/2}$, and

(3) for interaction effects,

$(\alpha_i^*(\beta_{jm}) \mid X_{ji}X_{mi} = -1) = -(4\sum 3^{k-2})^{-1/2}$,
$(\alpha_i^*(\beta_{jm}) \mid X_{ji}X_{mi} = 0) = 0$, and
$(\alpha_i^*(\beta_{jm}) \mid X_{ji}X_{mi} = 1) = (4\sum 3^{k-2})^{-1/2}$.

Note that $\sum_{i=1}^{n} \alpha_i^{*2} = 1$, which will be required for later statements and causes no loss of generality.

It is important to recognize that the contrast coefficients are closely related to the design variable values. For linear effects, the coefficients are proportional to the design levels $X_{ji}$. The coefficients for interaction effect $\beta_{jm}$ are proportional to the values $X_{ji}X_{mi}$ at each observation *i*. For the quadratic effect $\beta_{jj}$, the contrast coefficients are proportional to $X_{ji}^2$ - R, where R is a constant which centers the squared values.

The residual contrasts may be obtained by multiplying the model effect contrast coefficients for all possible pairs not in the model, i.e., all (linear, quadratic), (linear, interaction), (interaction, interaction), and (interaction, quadratic) pairs. The entire set of

$$r = 3^k - (2k + [k(k-1)/2] + 1)$$

residual contrasts may be obtained in this way. Thus, the residual contrasts are orthogonal to the model effect contrasts and have the properties ( 2.4 ) and ( 2.3 ) as listed above. Property ( 2.2 ) only requires that the contrast coefficients be standardized. As for properties ( 2.5 ) - ( 2.7 ), we employ the fact that $X_{ji} \propto \alpha_i^*(\beta_j)$ to recognize that for some constant $C_1$,

$$\sum_{i=1}^{n} \alpha_{gi} X_{ji} = C_1 \sum_{i=1}^{n} \alpha_{gi}\alpha_i^*(\beta_j) = 0,$$

and likewise for constants $C_2$ and $C_3$, $X_{ji}X_{mi} \propto \alpha_i^*(\beta_{jm})$ yields

$$\sum_{i=1}^{n} \alpha_{gi} X_{ji} X_{mi} = C_2 C_3 \sum_{i=1}^{n} \alpha_{gi}\alpha_i^*(\beta_{jm}) = 0.$$

Finally, $X_{ji}^2$ - R $\propto \alpha_i^*(\beta_{jj})$ and a constant $C_4$ imply that $C_4\, \alpha_i^*(\beta_{jj})$ - R = $X_{ji}^2$, so

$$\sum_{i=1}^{n} \alpha_{gi} X_{ji}^2 = C_4 \sum_{i=1}^{n} \alpha_{gi}\alpha_i^*(\beta_{jj}) - R \sum_{i=1}^{n} \alpha_{gi} = 0.$$

The result is that all properties required by Box for residual contrasts hold for 3 level factorials.

## 2.3 The Presence of Measurement Error in a Design for a Second Order Model

The following results extend to all data sets capable of estimating second order models. If measurement error is present in the system, the relationship between the design levels ($X_{ji}$) and the true unobserved values of the design variables ($x_{ji}$) is

$$X_{ji} = x_{ji} - u_{ji}, \quad i = 1, 2, ..., n, \text{ and } j = 1, 2, ..., k,$$

$$E[u_{ji}] = 0 \text{ and } Var[u_{ji}] = \sigma_j^2.$$

In the case of a second order model, there are further properties required for unbiased estimates of model effect contrast variances. Consider the variance of an estimated contrast

$$V(L) = \sum_{i=1}^{n} \alpha^{*\,2}_{\,i}\sigma_i^2$$

and the usual estimate of this quantity when $\sum_{i=1}^{n} \alpha^{*2}_i = 1$,

$$\hat{V}(L) = s_r^2 \sum_{i=1}^{n} \alpha^{*2}_i = s_r^2.$$

It is no longer the case that $s_r^2$ is an unbiased estimate of $\sigma_0^2$, since

$$E[s_r^2] = 1/r\ E[\sum_{g=1}^{r} (\sum_{i=1}^{n} \alpha_{gi} y_i)^2] = 1/r\ \{\sum_{i=1}^{n} (\sum_{g=1}^{r} \alpha_{gi}^2)\sigma_i^2 + \sum_{g=1}^{r} (\sum_{i=1}^{n} \alpha_{gi} E[y_i])^2\}.$$

From property ( 2.1 ) of residual contrasts and ( 1.9 ),

$$\sum_{i=1}^{n} \alpha_{gi} E[y_i] = 0 \Rightarrow \sum_{i=1}^{n} \alpha_{gi} (E[y_i|\underline{X}_i] + \mathbf{B}) = 0 \Rightarrow \sum_{i=1}^{n} \alpha_{gi} E[y_i|\underline{X}_i] = 0, \text{ since } \mathbf{B} \sum_{i=1}^{n} \alpha_{gi} = 0.$$

This simplifies the expected value of the residual variance estimate to

$$E[s_r^2] = 1/r\ \{\sum_{i=1}^{n} (\sum_{g=1}^{r} \alpha_{gi}^2)\sigma_i^2\}.$$

It follows that the additional requirement for $E[\hat{V}(L)] = V(L)$ is for

$E[s_r^2 \sum_{i=1}^{n} \alpha^{*2}_i] - \sum_{i=1}^{n} \alpha^{*2}_i \sigma_i^2 = 0$, or, since $\sum_{i=1}^{n} \alpha^{*2}_i = 1$,

$$(2.8) \quad \sum_{i=1}^{n} [(\sum_{g=1}^{r} \alpha_{gi}^2) - r\alpha_i^{*2}]\sigma_i^2 = 0.$$

Because of the general notation for var[$y_i$] when $y_i$ is modeled by a polynomial of degree $d$ (see equation 1.12), we know that $\sigma_i^2$ is a polynomial function of degree $2d$ - 2 in the designed factor levels, so that ( 2.8 ) is satisfied iff

$$(2.9) \quad \sum_{i=1}^{n} [(\sum_{g=1}^{r} \alpha_{gi}^{2}) - r\alpha_i^{*2}] = 0,$$

$$(2.10) \quad \sum_{i=1}^{n} [(\sum_{g=1}^{r} \alpha_{gi}^{2}) - r\alpha_i^{*2}]X_{ji} = 0, \forall j,$$

$$(2.11) \quad \sum_{i=1}^{n} [(\sum_{g=1}^{r} \alpha_{gi}^{2}) - r\alpha_i^{*2}]X_{ji}X_{mi} = 0, \forall j \neq m, \text{ and}$$

$$(2.12) \quad \sum_{i=1}^{n} [(\sum_{g=1}^{r} \alpha_{gi}^{2}) - r\alpha_i^{*2}]X_{ji}^{2} = 0, \forall j.$$

These four properties (( 2.9) - ( 2.12)) lead to the following result:

Theorem 1: *For any orthogonal design capable of estimating a second order model, the bias in every estimate of model coefficient variance is a function of the squared design levels.*

Proof: Because of property ( 2.2 ) and the requirement $\sum_{i=1}^{n} \alpha^{*2}_{i} = 1$, ( 2.9 ) is satisfied. In order to see that ( 2.10 ) and ( 2.11 ) hold, recall the relationship between model effect contrast coefficients ($\alpha_i^{*}$) and design values ($\underline{X}_i$). It is evident that $\alpha_i^{*2}$ is a function of even powers of design values. Specifically,

$\alpha_i^{*2}(\beta_j) \propto X_{ji}^{2}$,

$\alpha_i^{*2}(\beta_{jm}) \propto X_{ji}^{2} X_{mi}^{2}$, and

$\alpha_i^{*2}(\beta_{jj}) \propto X_{ji}^{4} - 2R\, X_{ji}^{2} + R^2$.

It follows by the construction of the residual contrast coefficients that $\alpha_{gi}^{2}$, g = 1, ..., r, are also functions of even powers of the design values. Now consider the left-hand side of the expressions in ( 2.10 ) and ( 2.11 ). These expressions are proportional to odd design moments. Since odd design moments for a full factorial design are always zero (notice that $x_i = x_i^{2k+1}$ and $x_i^2 = x_i^{2k}$ for $k$ = 1,2, 3 ...), both ( 2.10 ) and ( 2.11 ) are satisfied by $3^k$ factorial designs. The odd design moment of a CCD are also zero, since the designs are constructed to be orthogonal as well.

However, the same reasoning implies that the left-hand side of ( 2.12 ) is equivalent to an even design moment. An even design moment is not zero for any interesting design; i.e., for any design other than a set of center runs. Therefore, the bias in every estimate of model coefficient variance is a function of the squared design values.

The effect of this bias for two specific designs will be demonstrated in sections 2.3.1 and 2.3.3.

### 2.3.1 Example - $3^2$ Factorial Design

Consider a $3^2$ factorial design for which both design variables contain measurement error. The model matrix for a quadratic model using this design is

$$\begin{bmatrix} 1 & -1 & -1 & 1 & 1 & 1 \\ 1 & -1 & 0 & 0 & 1 & 0 \\ 1 & -1 & 1 & -1 & 1 & 1 \\ 1 & 0 & -1 & 0 & 0 & 1 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 & 1 \\ 1 & 1 & -1 & -1 & 1 & 1 \\ 1 & 1 & 0 & 0 & 1 & 0 \\ 1 & 1 & 1 & 1 & 1 & 1 \end{bmatrix} \qquad (2.13)$$

Using the expression for Var[$y_i$] from (1.10), it is evident that $\hat{V}(L)$ is unbiased iff

$$\sum_{i=1}^{n} [(\sum_{g=1}^{r} \alpha_{gi}^2) - r\alpha_i^{*2}]\times$$
$$[\sigma_0^2 + \sigma_1^2(\beta_1^2 + \beta_{12}^2 X_{2i}^2 + 4\beta_{11}^2 X_{1i}^2) + \sigma_2^2(\beta_2 + \beta_{12}^2 X_{1i}^2 + 4\beta_{22}^2 X_{2i}^2)$$
$$+ 2\rho_{12}\sigma_1\sigma_2 (\beta_1\beta_2 + \beta_1\beta_{12}X_{1i} + 2\beta_1\beta_{22} X_{2i} + \beta_2\beta_{12}X_{2i} + \beta_{12}^2 X_{1i}X_{2i} + 2\beta_{12}\beta_{22}X_{2i}^2 + 2\beta_2\beta_{11}X_{1i}$$
$$+ 2\beta_{11}\beta_{12}X_{1i}^2 + 4\beta_{11}\beta_{22}X_{1i}X_{2i}) + 2\beta_{11}\sigma_1^4 + 2\beta_{22}\sigma_2^4] = 0,$$

where K is a constant of higher order moments for $u_1$ and $u_2$. The equation above can be separated into the following parts:

(i) $[\sigma_0^2 + \sigma_1^2\beta_1^2 + \sigma_2^2\beta_2 + 2\rho_{12}\sigma_1\sigma_2\beta_1\beta_2 + 2\beta_{11}\sigma_1^4 + 2\beta_{22}\sigma_2^4] \sum_{i=1}^{n} [(\sum_{g=1}^{r} \alpha_{gi}^2) - r\alpha_i^{*2}]$,

(ii) $[2\rho_{12}\sigma_1\sigma_2(\beta_1\beta_{12} + 2\beta_2\beta_{11})] \sum_{i=1}^{n} [(\sum_{g=1}^{r} \alpha_{gi}^2) - r\alpha_i^{*2}]X_{1i,}$

(iii) $[2\rho_{12}\sigma_1\sigma_2(\beta_2\beta_{12} + 2\beta_1\beta_{22})] \sum_{i=1}^{n} [(\sum_{g=1}^{r} \alpha_{gi}^2) - r\alpha_i^{*2}]X_{2i}$,

(iv) $[2\rho_{12}\sigma_1\sigma_2(\beta_{12}^2 + 4\beta_{11}\beta_{22})] \sum_{i=1}^{n} [(\sum_{g=1}^{r} \alpha_{gi}^2) - r\alpha_i^{*2}]X_{1i}X_{2i}$,

(v) $[4\sigma_1^2\beta_{11}^2 + \sigma_2^2\beta_{12}^2 + 2\rho_{12}\sigma_1\sigma_2\beta_{11}\beta_{12}] \sum_{i=1}^{n} [(\sum_{g=1}^{r} \alpha_{gi}^2) - r\alpha_i^{*2}]X_{1i}^2$, and

(vi) $[4\sigma_2^2\beta_{22}^2 + \sigma_1^2\beta_{12}^2 + 2\rho_{12}\sigma_1\sigma_2\beta_{22}\beta_{12}] \sum_{i=1}^{n} [(\sum_{g=1}^{r} \alpha_{gi}^2) - r\alpha_i^{*2}]X_{2i}^2$.

Based on the previous work, (i), (ii), (iii), and (iv) are all zero. As a result, the bias in $\hat{V}(L)$ is a function of the squared design levels, as well as $\sigma_1^2$, $\sigma_2^2$, $\rho_{12}$, $\beta_{12}$, $\beta_{11}$ and $\beta_{22}$. The squared bias of the estimated variance for each model effect contrast is listed in Table 2.1. To calculate the bias involved in each contrast, the necessary contrast coefficients are formed for both model effects and residuals. The effect contrasts are as follows:

$\underline{\alpha}(\beta_0)'$ = 1/3 * {1, 1, 1, 1, 1, 1, 1, 1, 1},

$\underline{\alpha}(\beta_1)'$ = 0.408248 * { -1, -1, -1, 0, 0, 0, 1, 1, 1},

$\underline{\alpha}(\beta_2)'$ = 0.408248 * { -1, 0, 1, -1, 0, 1, -1, 0, 1},

$\underline{\alpha}(\beta_{12})'$ = .5 * { 1, 0, -1, 0, 0, 0, -1, 0, 1},

$\underline{\alpha}(\beta_{11})'$ = 0.2357023 * { 1, 1, 1, -2, -2, -2, 1, 1, 1}, and

$\underline{\alpha}(\beta_{22})'$ = 0.2357023 * { 1, -2, 1, 1, -2, 1, 1, -2, 1}.

The residual contrasts satisfy all properties ( 2.9 ) - ( 2.12 ) and are as follows:

$\underline{\alpha}_1'$ = 0.288675 * { -1, 2, -1, 0, 0, 0, 1, -2, 1 },

$\underline{\alpha}_2'$ = 0.288675 * { -1, 0, 1, 2, 0, -2, -1, 0, 1 },

$\underline{\alpha}_3'$ = 1/6 * {1, -2, 1, -2, 4, -2, 1, -2, 1}.

Table 2.1 Squared Bias Terms for $\hat{V}(\alpha(\beta))$ from a $3^2$ Factorial Design

| Contrast | Squared Bias* |
|---|---|
| $\alpha(\beta_1)$ | $(-4/3 \cdot K1 - 1/3 \cdot K2)^2$ |
| $\alpha(\beta_2)$ | $(-1/3 \cdot K1 - 4/3 \cdot K2)^2$ |
| $\alpha(\beta_{12})$ | $(-4/3 \cdot K1 - 4/3 \cdot K2)^2$ |
| $\alpha(\beta_{11})$ | $(2/3 \cdot K1 - 1/3 \cdot K2)^2$ |
| $\alpha(\beta_{22})$ | $(-1/3 \cdot K1 + 2/3 \cdot K2)^2$ |

*$K1=4\sigma_1^2\beta_{11}^2+\sigma_2^2\beta_{12}^2+2\rho_{12}\sigma_1\sigma_2\beta_{11}\beta_{12}$, $K2=4\sigma_2^2\beta_{22}^2+\sigma_1^2\beta_{12}^2+2\rho_{12}\sigma_1\sigma_2\beta_{22}\beta_{12}$

### 2.3.2 CCD Example

To satisfy the Box requirements for a CCD, the contrast set is more difficult to express due to unequal replications of design level combinations and possible unequal spacing for those levels (-*d*, -1, 0, 1, *d*). General expressions for all model effect and residual contrasts are given for two factor CCDs in Appendix A and for three factor CCDs in Appendix B. Table 2.2 indicates the amount of bias associated with each factor in a CCD with $d = 2$ and $n_c = 1$.

It is evident from Table 2.1 and Table 2.2 that bias is a problem in both designs The squared bias is greater for the CCD. However, the CCD analyzed has arbitrarily placed axial points and only one center run. No attempt has been made to minimize the squared bias with respect to the value of the axial point.

Table 2.2 Squared Bias Terms for $\hat{V}(\alpha(\beta))$ from a CCD with *d* = 2 and $n_c$ = 1.

| Contrast | Squared Bias* |
|---|---|
| $\alpha(\beta_1)$ | $(-17/3 \cdot K1 + 7/3 \cdot K2)^2$ |
| $\alpha(\beta_2)$ | $(7/3 \cdot K1 + 17/3 \cdot K2)^2$ |
| $\alpha(\beta_{12})$ | $(1/3 \cdot K1 + 1/3 \cdot K2)^2$ |
| $\alpha(\beta_{11})$ | $(-17/3 \cdot K1 + 51/45 \cdot K2)^2$ |
| $\alpha(\beta_{22})$ | $(44/15 \cdot K1 - 52/15 \cdot K2)^2$ |

*$K1=4\sigma_1^2\beta_{11}^2 + \sigma_2^2\beta_{12}^2 + 2\rho_{12}\sigma_1\sigma_2\beta_{11}\beta_{12}$, $K2=4\sigma_2^2\beta_{22}^2 + \sigma_1^2\beta_{12}^2 + 2\rho_{12}\sigma_1\sigma_2\beta_{22}\beta_{12}$

## 2.4 $\hat{V}(L)$ for a CCD with multiple center runs

The single center run in the previous example allowed for the estimate of the overall variance to be stated in terms of residual contrasts. For $n_c > 1$, a new $\hat{V}(L)$ expression is needed which incorporates pure error from the replicated point. The estimate of the overall variance is now

$$s^2 = (r + n_c - 1)^{-1}\{ ( \sum_{g=1}^{r} [( \sum_{i=1}^{n-n_c} \alpha_{gi}y_i) + \alpha_{gn_c}\bar{y}_{n_c} ]^2) + \sum_{i=n-n_c+1}^{n} (y_i - \bar{y}_{n_c})^2 \},$$

where $\bar{y}_{n_c}$ is the average response for the center runs. This leads to a bias expression of

$$E(\hat{V}(L)) - V(L) = \sum_{i=1}^{n} [(r + n_c - 1)\, \alpha_i^{*2} - \sum_{g=1}^{r} \alpha_{gi}^2]\sigma_i^2 - (n_c - 1)\, \sigma_{n_c}^2 ,$$

where $\sigma_{n_c}^2$ is the variance at a center run. Bias for CCDs with $n_c > 1$ would be calculated using this expression.

## 2.5 Conclusions

The focus of this chapter is to characterize the effect of ME on coefficient estimates in an analysis ignoring ME in the design factors. The problem appears as a bias in the variance estimate for the coefficients. The form of this bias applies to coefficients estimated by the contrasts outlined in this chapter. The impact of this bias on the choice of axial points for two and three factor CCDs will be explored in Chapter 3.

# 3. Optimal Values for Axial Points of Two and Three Factor CCDs in the Presence of ME

Several factors must be considered in the determination of an optimal value for the axial point of a CCD with ME in the design levels. First of all, there is a different bias value associated with the estimated variance of each model effect. This indicates that the optimal value of an axial point may not be the same for the estimation of each coefficient. Also, the model coefficients themselves are involved in the bias terms, so that knowledge of the true coefficient values is necessary to determine optimal values. This may be simplified slightly by considering ratios of coefficients rather than actual coefficient values, i.e., $\beta_{12}/\beta_{11}=3$ rather than $(\beta_{12}, \beta_{11}) = (1.5, 0.5)$, (3, 1), etc. Other considerations include the number of center runs, the number of factors in the experiment, and the number of design factors affected by ME in the particular study. The CCDs in this chapter contain ME in a single factor and include a single center run. Optimal values for axial points are discussed for two- and three-factor CCDs in this chapter.

## 3.1 Two-Factor CCDs

An initial investigation focused on a two factor, second order model. The nine-point design was a single center run CCD with ME in one design factor. The squared bias of the variance estimate was minimized for each model effect assuming a common value for the axial points of both factors. The squared bias term in this situation is

$$B = (4\sigma_1^2 \beta_{11}^2 \cdot \sum_{i=1}^{9} [(\sum_{g=1}^{3} \alpha_{gi}^2) - 3\alpha_i^{*2}]X_{1i}^2 + \beta_{12}^2 \cdot \sum_{i=1}^{9} [(\sum_{g=1}^{3} \alpha_{gi}^2) - 3\alpha_i^{*2}]X_{2i}^2)^2, \quad (3.1)$$

where $\sum_{g=1}^{3} \alpha_{gi}^2$, $\alpha_i^{*2}$, and $\underline{X}_j^2$, (j= 1, 2) all contain *d*, the value of the axial point. Recall that $\alpha_i^{*2}$ are the squared model effect contrast coefficients, and $\alpha_{gi}^2$ are the squared residual contrast coefficients. Thus equation 3.1 is a function of the value of the axial point through the model effect of interest, all residual effects, and the squared design levels of each factor in the design. Notice that the presence of ME in only one of the factors simplifies the bias from the more general expressions (v) and (vi) in Section 2.4, so that the squared bias depends only on the coefficients $\beta_{11}$ and $\beta_{12}$.

Using the FindMinimum function in Mathematica® (1994), the squared bias expression was minimized across a range of possible values for the axial points ( $d \in (0,4)$). The restriction to this range was chosen because in some cases the squared bias for a certain model effect was minimized as $d \to \infty$. The values of $d$ which minimize expression 3.1 for several ratios of $\beta_{11}/\beta_{12}$ can be found in Table 1.1 of Appendix B. However, trends among these values are hard to locate. Plots of the squared bias for each ratio of true coefficient values $\beta_{11}/\beta_{12}$ are more informative, so they are presented in Figure 3.1. The plots represent squared bias as a function of *d*. Each plot is labeled with the model coefficients used in the squared bias expression, which are represented by b12 and b11. For example, the plot in the lower left corner of the figure shows the squared bias expression when $\beta_{12}$= 1 and $\beta_{11}$= 4. In Figure 3.1, *d* is constrained to be the same value for both design factors ($X_1$ and $X_2$). Most plots do not include the entire range of (0,4) on the x axis, because the minimum *d* for all four contrasts of interest is inside that range. Each plot includes the contrasts representing $\beta_1$, $\beta_2$, $\beta_{11}$, and $\beta_{22}$. Because the value of $\sum_{i=1}^{9} \alpha_i^{*2}(\beta_{12})X_{ji}^2$ is 0 for j = 1, 2, the squared bias for the interaction coefficient does not change for different values of $\beta_{11}/\beta_{12}$. This result is intuitive, since the axial points do not contribute to the estimation of interaction effects. The model effect for interaction is not included in the tables and figures for this reason.

It is important to note that these contrasts are orthogonal and created sequentially, so that $\alpha(\beta_{22})$ actually represents the effect of $X_2^2$ beyond all other effects in the model. This could be an explanation for the strange behavior of the squared bias for $\alpha(\beta_{22})$. There is no global optimal value for the axial points across all model effects. However, with the exception of estimation of the coefficient $\beta_{22}$, the plots seem to indicate that a value near $d = \sqrt{2} = 1.414$ is a good compromise value across all coefficient estimates. This value of *d* creates a rotatable CCD, which is beneficial for other reasons noted in previous chapters.

In some cases, more specific estimation goals may be of interest. If the coefficients for linear effects ($\beta_1$, $\beta_2$) are of more importance than the quadratic effects, the plots suggest that axial points near ±1 are best in most situations. This design is a $3^2$ factorial. There is a range of values for which the squared bias is relatively unchanged for either $\beta_1$ or $\beta_2$, depending on the magnitude of the interaction effect. For example, when $\beta_{12}$ = 1 and $\beta_{11}$ = 2, the squared bias is basically minimized across a range of values for the axial points (1.0, 1.5). If the coefficient of interest is quadratic ($\beta_{11}$), the plots indicate that axial points between ±1.5 and ±2.2 are more beneficial.

However, the constraint that both factors have the same value for axial points may defeat the purpose of specifying the presence of ME in only $X_1$. It is possible that the value of the axial point for the factor containing ME should differ from the other factors included in the design.

Considering the same two factor, single center run situation, it was decided to allow the value of the axial points to differ for the two factors. The value $d1$ represents the value of the axial point for $X_1$ (the factor affected by ME), and $d2$ represents the value of the axial point for $X_2$. The squared bias expressions generated with $d1$ and $d2$ were too complex to allow any conclusions when minimizing with respect to both axial point values simultaneously. For this reason, the value of $d2$ was set at two different values (1, $\sqrt{2}$) which correspond to a $2^3$ factorial and a rotatable CCD. The squared bias expression was plotted in each situation with respect to $d1$. Figure 3.2 and Figure 3.3 show these results. Tables 1.2 and 1.3 in Appendix C include $d1$ values which minimize the squared bias for each of the contrasts represented by curves in Figure 3.2 and Figure 3.3. In some cases, there are two values for the axial points which minimize the squared bias over the range (0, 4).

Considering Figure 3.2, it is apparent that two situations occur. When the quadratic effect ($\beta_{11}$) is larger than the interaction effect ($\beta_{12}$), the best overall choice for $d1$ is near or slightly greater than a value of 1. Since $d2$ is constrained to be 1 in this situation, the resulting design is practically a $3^2$ factorial. Thus a more conservative design (i.e., a smaller experiment within the design region) is in order when $d2$ is constrained to be 1 than when the axial points are a common value for all design factors. However, interest in specific model effects may lead to different axial point values. For instance, if $\beta_{11}$ is large in relation to $\beta_{12}$, and the effects of interest are the quadratic effects, axial points at ±1.3 are better than axial points at ±1. When the interaction effect is larger than the quadratic effect, the axial points for $X_1$ should be placed somewhere between 1 and 1.4.

Notice that when $d1$and $d2$ are not constrained to be the same number, the values for $d1$ are very different depending on the specified value of $d2$. Figure 3.3 shows the patterns for optimal $d1$ values when $d2 = \sqrt{2}$. For most coefficient ratios in this case, the optimal $d1$ would be one or near one. Notice that most of the values are less than or equal to $\sqrt{2}$, except for situations where the quadratic effect ($\beta_{11}$) does not exist. When the quadratic effect in $X_1$ is suspected to be larger than the interaction effect, the optimal value of the axial point for detecting the $\beta_{22}$ coefficient is to have the point include more center runs.

Unfortunately, there is no clear optimal value for the axial points of the factor containing ME. In almost all situations, however, the suggested axial point value is on the interior of a rotatable CCD. When an interaction effect is expected to be larger than the quadratic effect in $X_1$, the axial points should be closer to the edge of the design space than when the situation is reversed. Because of the difference in the optimal values for individual model effects, these results may be put to better use when targeting a specific effect of interest than when deciding on a best axial point for overall estimation.

## 3.2 Three Factor CCDs

Three factor single center run CCDs were also investigated for trends in optimal values for axial points. ME was present in $X_1$ only. The squared bias in this situation can be expressed as

$$B = (4\sigma_1^2 \beta_{11}^2 \cdot \sum_{i=1}^{15} [(\sum_{g=1}^{5} \alpha_{gi}^2) - 5\alpha_i^{*2}] X_{1i}^2 + \beta_{12}^2 \cdot \sum_{i=1}^{15} [(\sum_{g=1}^{5} \alpha_{gi}^2) - 5\alpha_i^{*2}] X_{2i}^2$$

$$+ \beta_{13}^2 \cdot \sum_{i=1}^{15} [(\sum_{g=1}^{5} \alpha_{gi}^2) - 5\alpha_i^{*2}] X_{3i}^2)^2. \qquad (3.2)$$

Similar to the two factor case, the expressions $\sum_{g=1}^{5} \alpha_{gi}^2$, $\alpha_i^{*2}$, and $\underline{X}_j^2$ (j = 1, 2, 3) are all functions of $d$ for the three factor situation. Notice that the bias expression is dependent only on $\beta_{11}^2$, $\beta_{12}^2$, and $\beta_{13}^2$. Tables 2.1 - 2.3 in Appendix B indicate the grid of ($\beta_{11}$, $\beta_{12}$, $\beta_{13}$) coefficient values explored for the three factor case. Figure 3.4 - Figure 3.9 contain plots for many of the coefficient combinations across a range of values for the axial points. Squared bias for the $\beta_1$, $\beta_2$, $\beta_3$, $\beta_{11}$, $\beta_{22}$, and $\beta_{33}$ contrasts is plotted. The value of $\sum_{i=1}^{9} \alpha_i^{*2} X_{ji}^2 = 0$, j=1, 2, 3, for all interaction effects ($\alpha^*(\beta_{kl})$, where k≠l), and so the optimal value of $d$ for $\alpha(\beta_{kl})$ is always 0. These model effects are not included in the tables and figures. If the squared bias expression did not have a minimum value in (0,6), then the value 6 is indicated in the table. Plots in the figures also include a range of (0, 6), although some ranges are smaller so that the plots are more detailed. Table 2.1 shows the optimal value of the axial point when a common $d$ is used for all three factors, while Tables 2.2 and 2.3 indicate optimal values of $d1$ for $d2 = 1$ and $d2 = \sqrt{3}$, respectively. In the three factor situation, $d2$ is the value of the axial point for the factors without measurement error. The $d2$ values chosen represent typical values in 3 factor designs (a $3^3$ fractional factorial and a nearly rotatable CCD). In each situation, an increase in the true value of $\beta_{11}$ had little effect on the optimal value of the axial points. For this reason, only $\beta_{11}$ values of 0 and 1 appear in the figures.

When all axial points have a common value for the three factors, the optimal $d$ is between 1 and 1.5. The contrast for $\beta_{33}$ is problematic for reasons similar to the problem with the $\beta_{22}$ contrast in the 2 factor case. Since it represents very little of the systematic variability in the response, the bias term is very unstable and gives little information. In the case of a common value for the axial points, the plots for various $\beta_{12}$ values were similar to $\beta_{13}$ values, so not all plots are shown in Figure 3.4 and Figure 3.5. Note that for all combinations of true coefficient values, the optimal $d$ is still smaller than $\sqrt[4]{8} \approx 1.68$, which is the value of the axial point of a rotatable 3 factor CCD.

When the value of the axial points for $X_1$ and $X_2$ are held at +/-1, the optimal $d1$ values range between 1 and 2. In situations where the true coefficients contain large interaction terms, the optimal values are pushed out closer to 2. The optimal values are pulled in near 1 when the quadratic coefficient dominates.

When the axial points for $X_1$ and $X_2$ are set at $\sqrt{3}$, most optimal $d1$ values are between 1 and 1.5, as in the common $d$ situation. This indicates that the points should be pulled to the interior of the design space for the factor containing ME.

There is no single value of the axial points which satisfies all conditions, but there are some general conclusions which can be drawn. A typical rotatable CCD is a good starting point for a design, but these plots suggest that putting the axial points in the interior of the design space for the factor containing ME is preferable to a fully rotatable CCD. This is especially beneficial if the experimenter feels that the quadratic effect in the ME factor will be quite large. For stronger interaction terms, conservative values for axial points for the ME factor are still worthwhile. A final reminder is that these results are based on an analysis approach to the estimation of the coefficients which ignores the ME in the design factors. More appropriate analysis techniques will be discussed in future chapters of the dissertation.

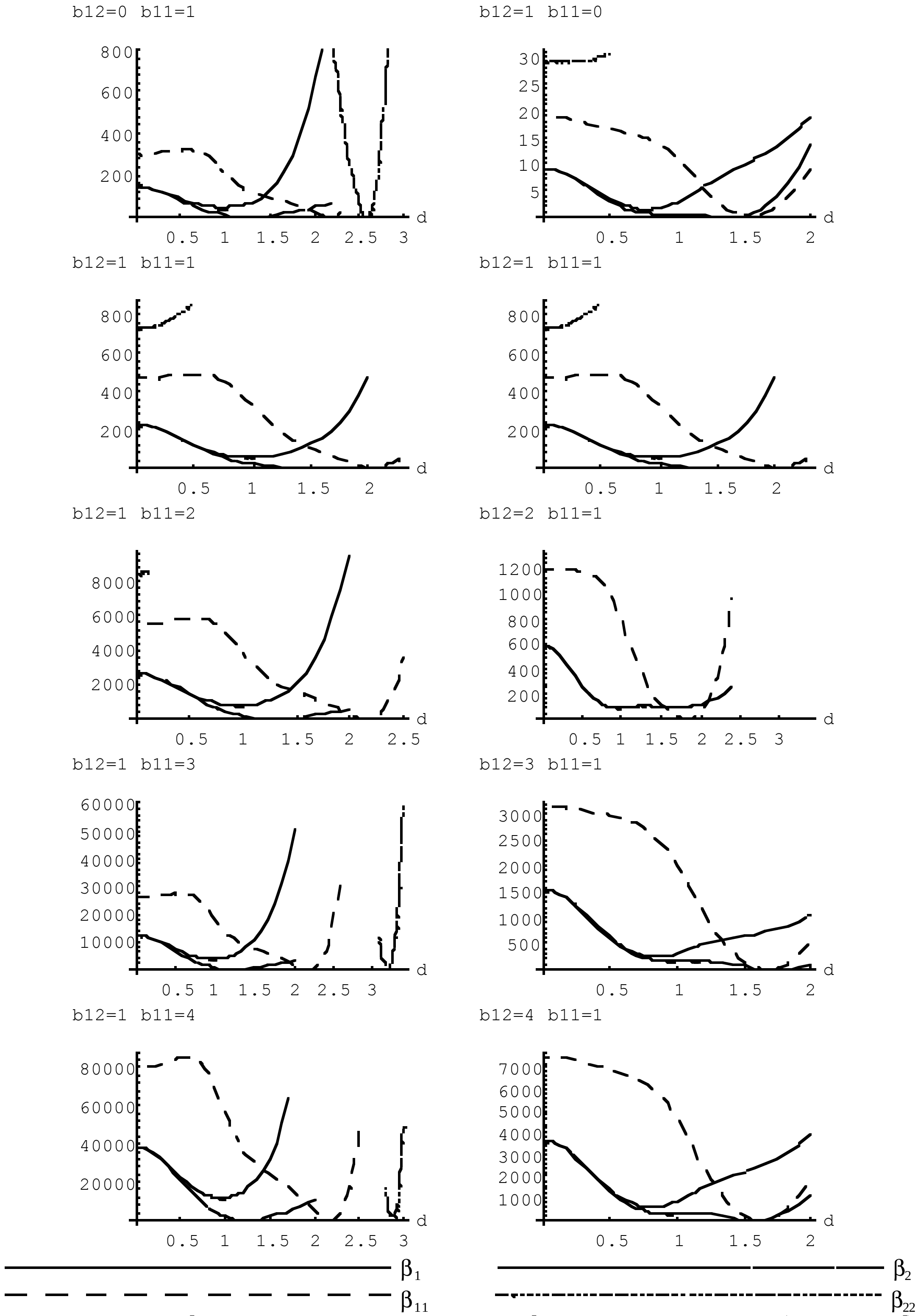

Figure 3.1 Squared Bias in Variance Estimate vs. *d* in a Two Factor CCD (Common *d*)

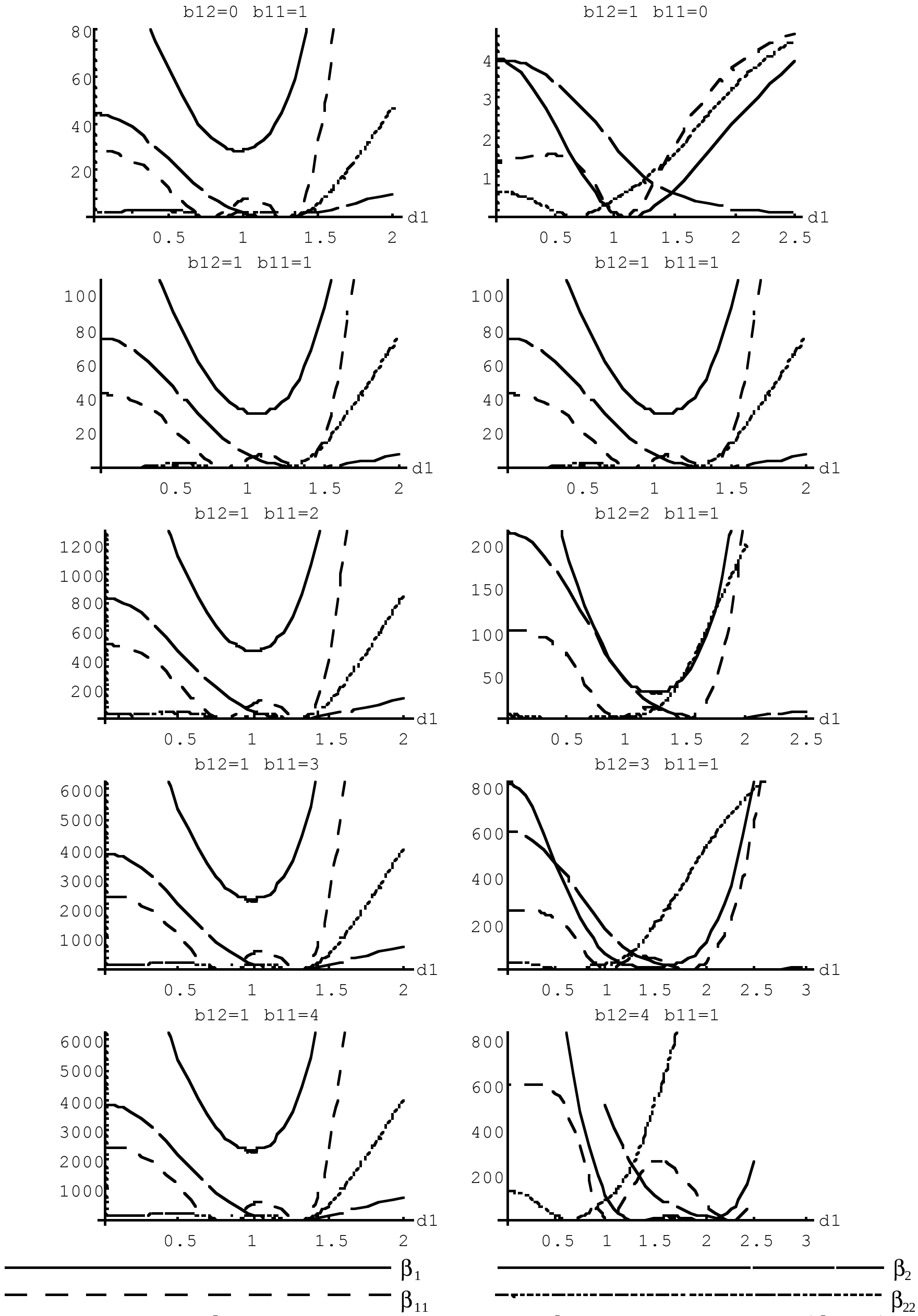


Figure 3.2 Squared Bias in Variance Estimate vs. *d* in a Two Factor CCD (*d*2 = 1)

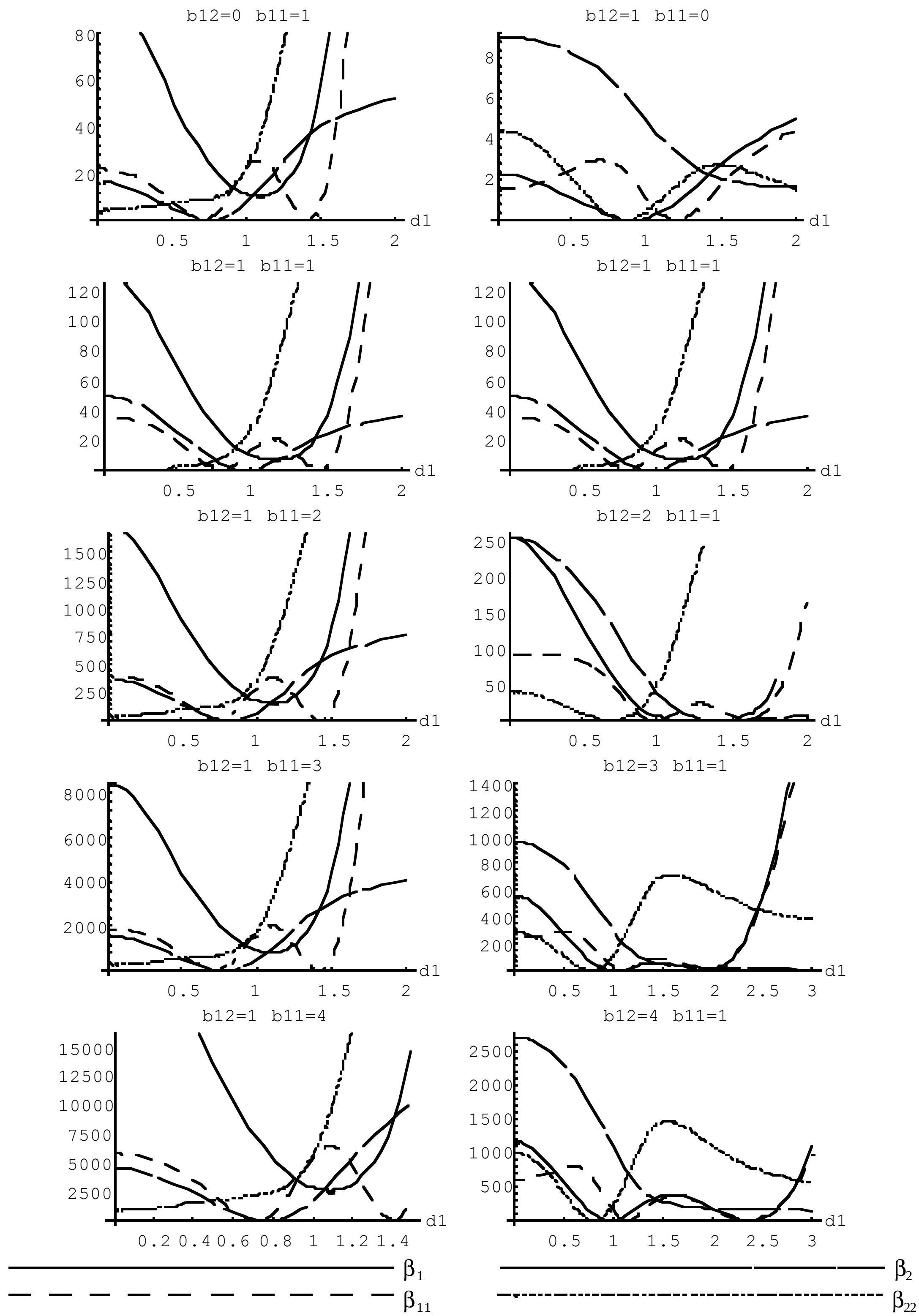


Figure 3.3 Squared Bias in Variance Estimate vs. *d* in a Two Factor CCD ($d2 = \sqrt{2}$)

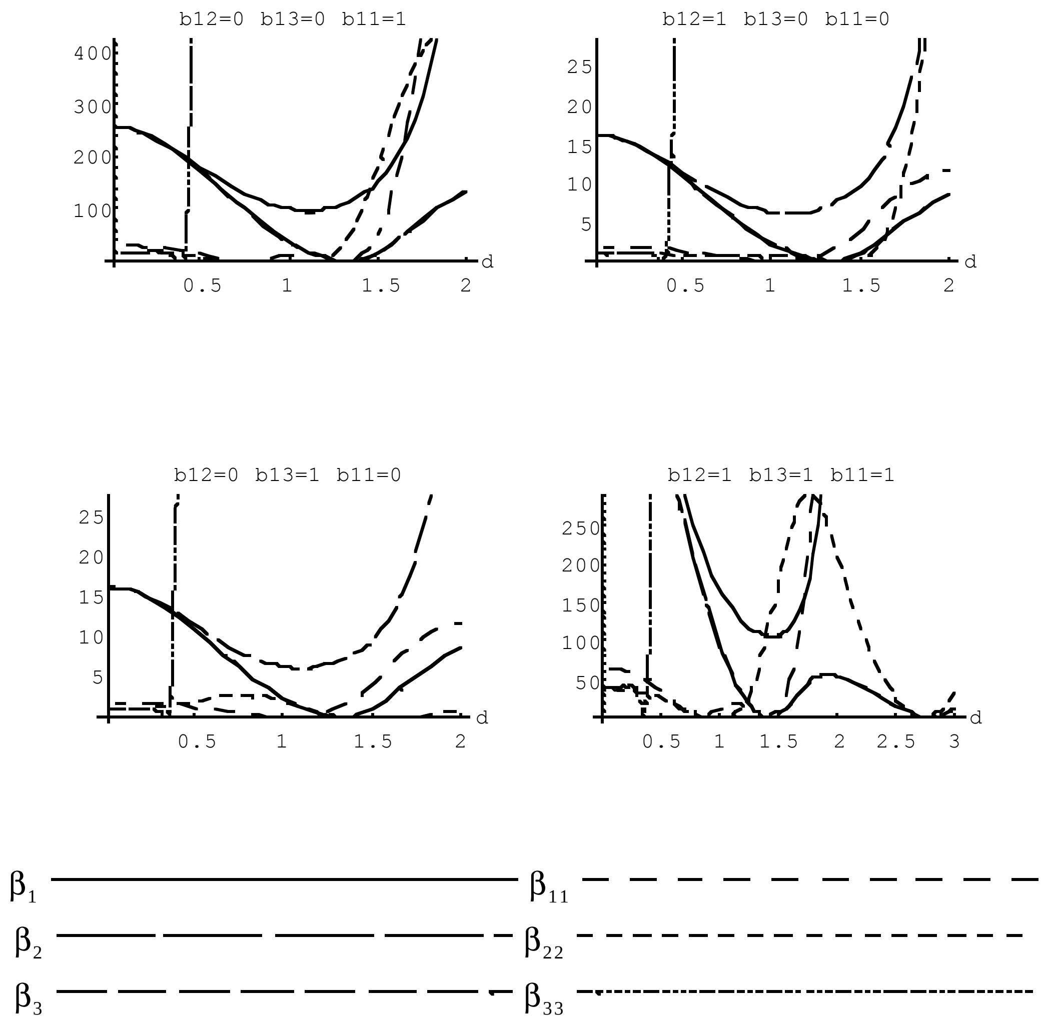


Figure 3.4 Squared Bias in Variance Estimate vs. *d* in a Three Factor CCD (Common *d*)

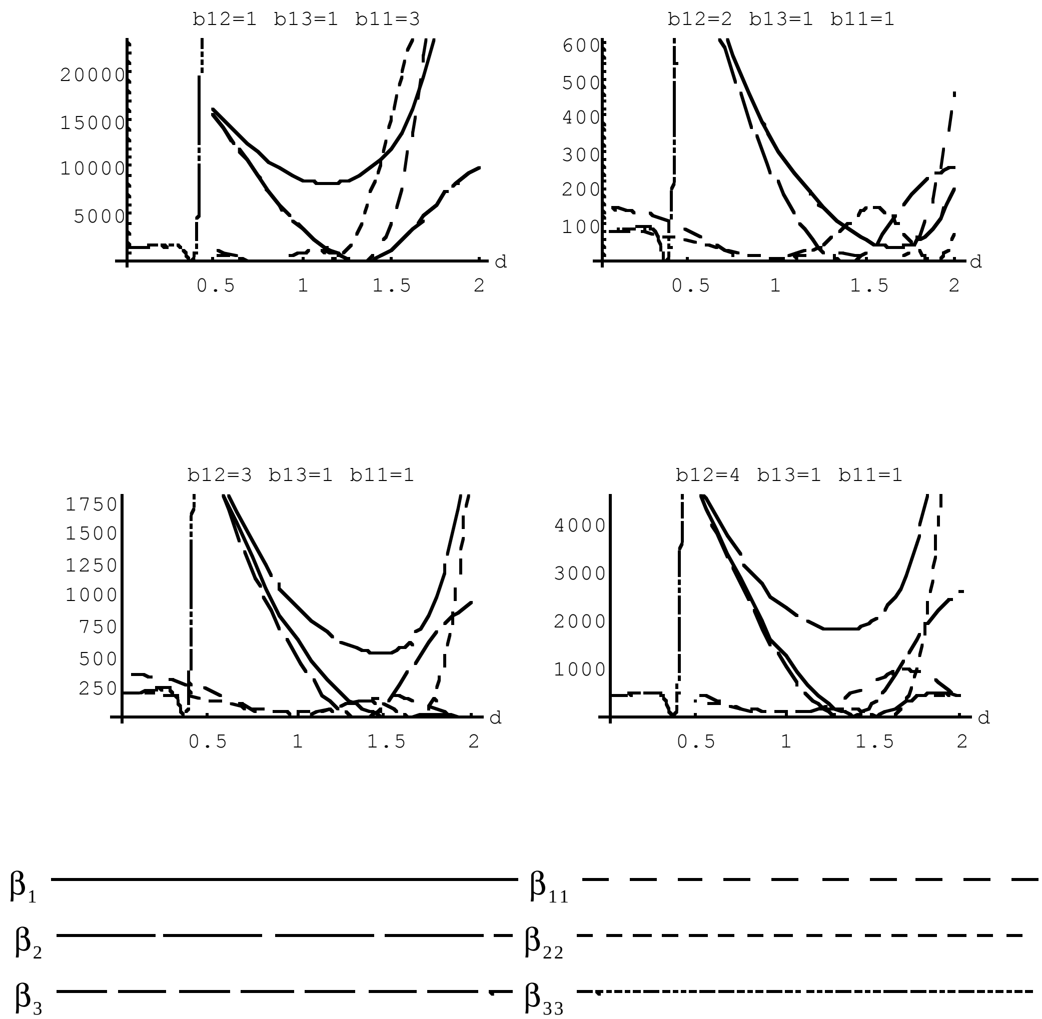


Figure 3.5 Squared Bias in Variance Estimate vs. *d* in a Three Factor CCD (Common *d*)

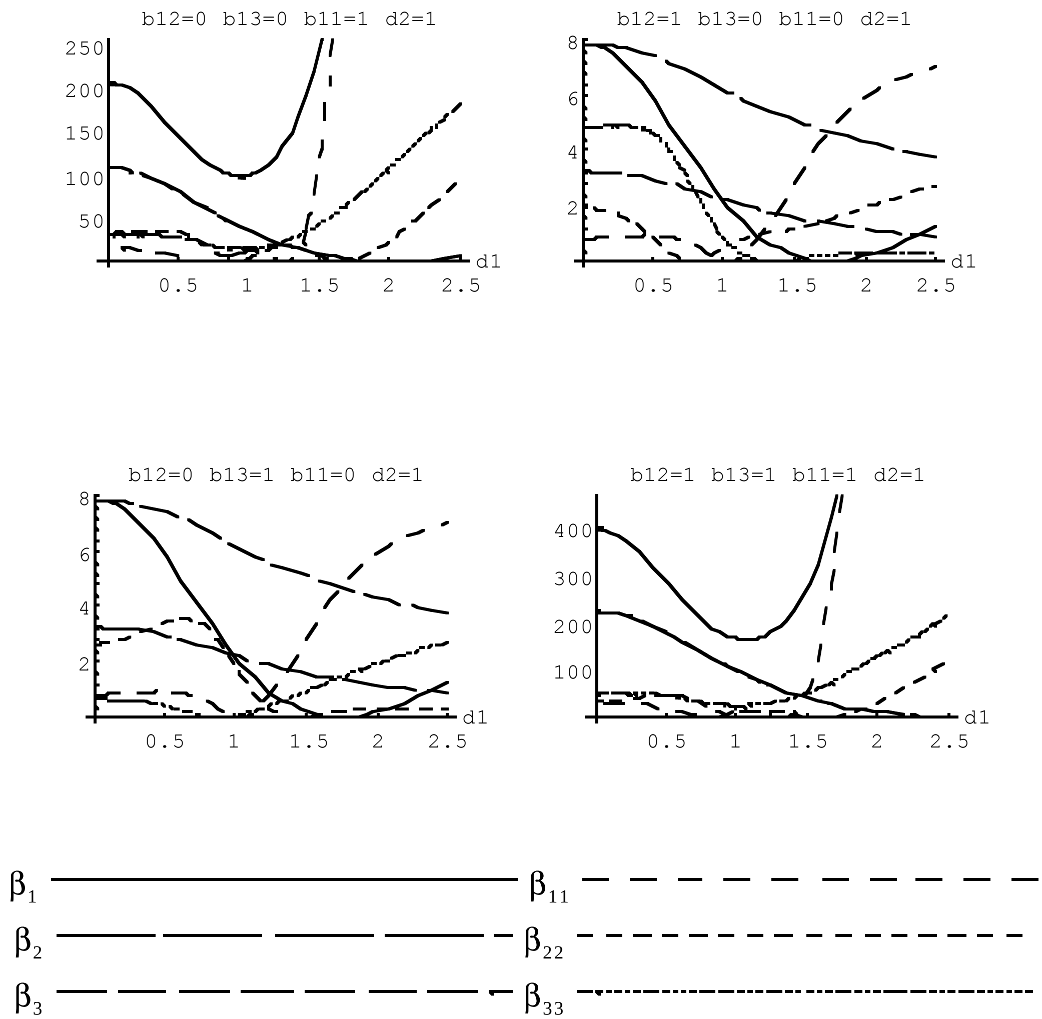


Figure 3.6 Squared Bias in Variance Estimate vs. *d* in a Three Factor CCD (*d*2 = 1)

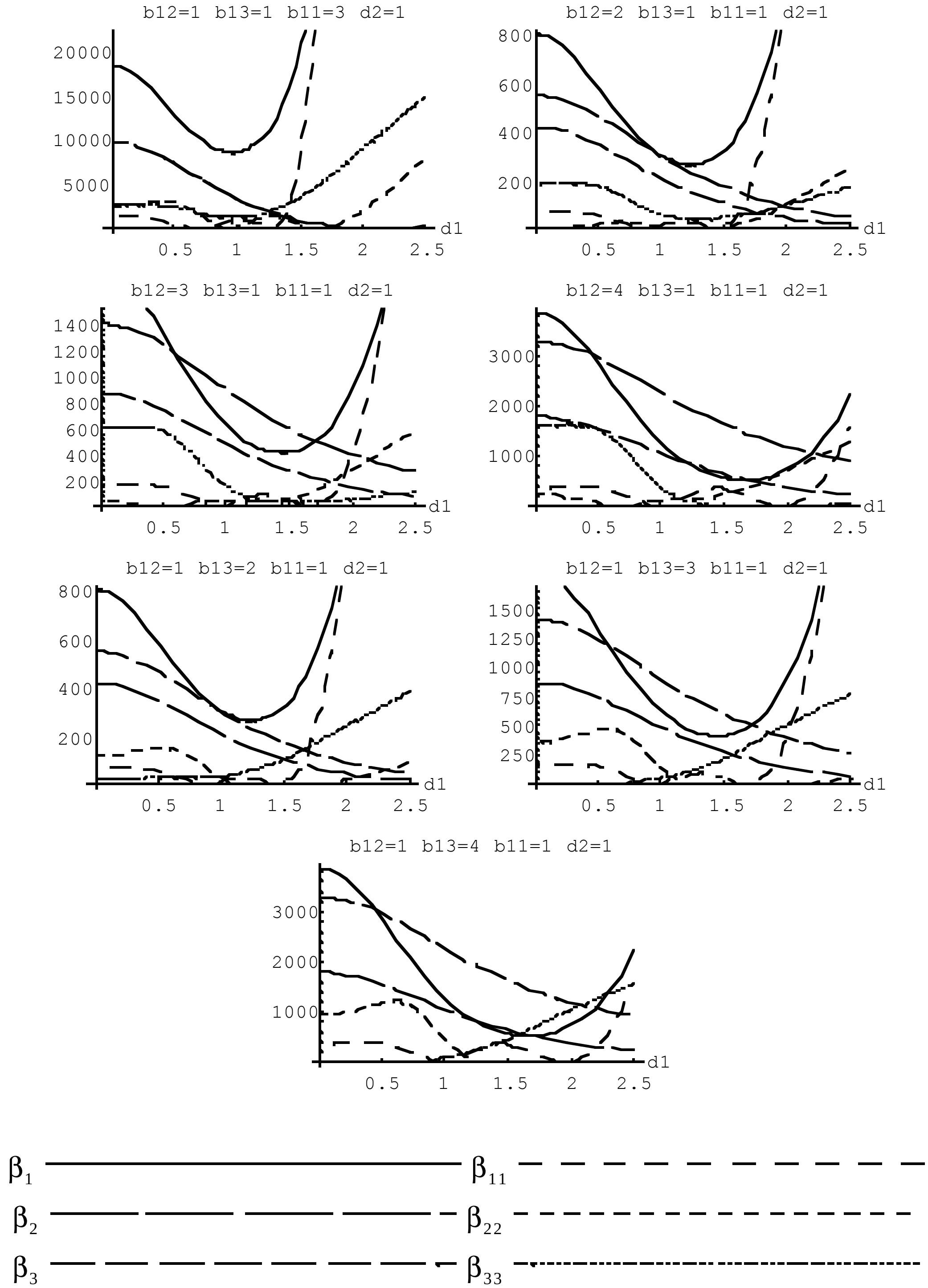


Figure 3.7 Squared Bias in Variance Estimate vs. *d* in a Three Factor CCD (*d*2 = 1)

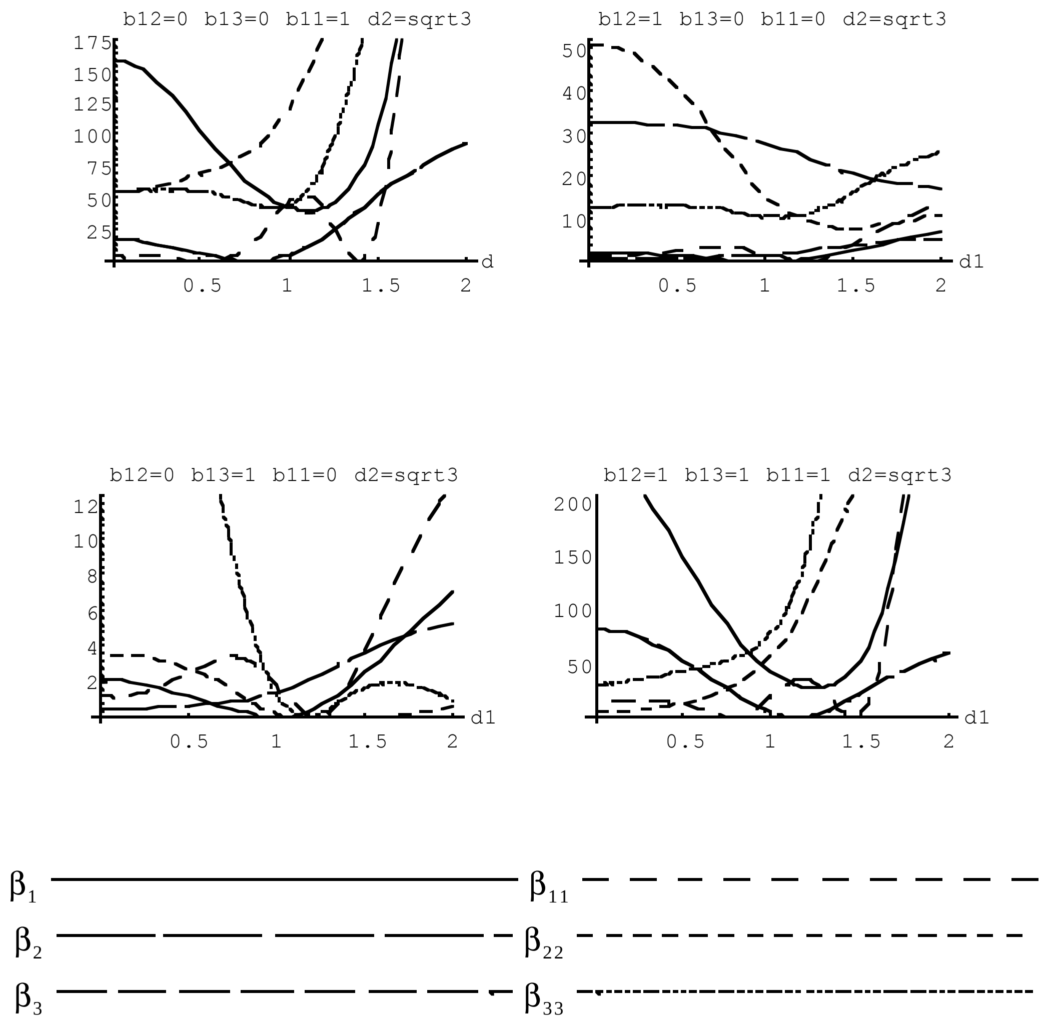


Figure 3.8 Squared Bias in Variance Estimate vs. *d* in a Three Factor CCD ($d2 = \sqrt{3}$)

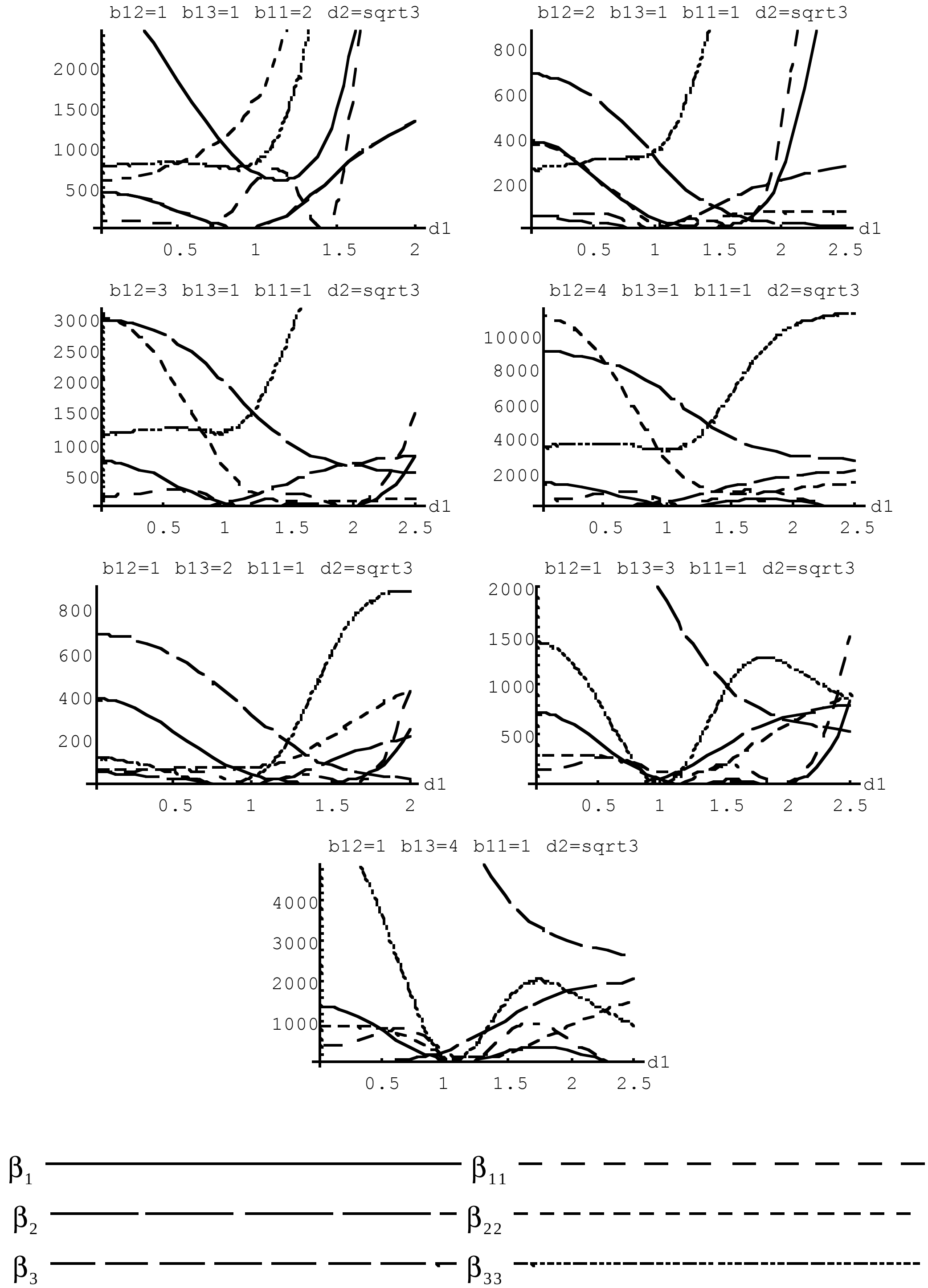


Figure 3.9 Squared Bias in Variance Estimate vs. *d* in a Three Factor CCD ($d2 = \sqrt{3}$)

# 4. The Analysis of Designs Involving ME

The ME literature contains no satisfactory benchmark for the amount of ME which is problematic in an OLS analysis of a second order system. For this reason, an exploration of the importance of ME to these systems is warranted. "Importance" will be quantified by addressing the following questions: (1) What is the appropriate approach to analyzing data sets in which ME is present in the designed experiment? Emphasis will be placed on those data sets with a quadratic relationship between *x* and *y*. (2) Is it possible that, for small magnitudes of ME, an analysis ignoring the added variability will estimate the model as well as an analysis incorporating the ME? (3) Along those same lines, at what point would one design improve upon another given equal ME in the system? A simulation of various ME systems supplies the answers to these questions. Two different analyses will be compared for the second order systems: OLS analysis will be considered the "naïve" analysis which ignores ME, and a second analysis will be presented as the correct approach to the ME problem. The beginning of this chapter will outline this analysis for first and second order models. Later sections will give the details of the simulations, as well as the results and conclusions from them.

## 4.1 The Correct Analysis of Designs with ME

### 4.1.1 First Order ME Models

Recall that the first order ME model presented in Chapter 1 (see equation 1.1) is known as a Berkson error model. Berkson error models are a special case in the class of regression models with random coefficients. For the first order model containing Berkson error, only the intercept coefficient is random (Carroll, Ruppert, and Stefanski, 1995). Consider the first order linear model with k regressors:

$$y_j = \beta_0 + \sum_{i=1}^{k} \beta_i x_{ij} + e_j,$$

$$\text{or } y_j = \beta_0 + \sum_{i=1}^{k} \beta_i X_{ij} + \sum_{i=1}^{k} \beta_i u_{ij} + e_j.$$

This expression can be rewritten in the notation of Longford (1993) as

$$y_j = \underline{X}'_j\underline{\beta} + \underline{X}'_j\underline{\gamma}_j + e_j, \qquad (4.1)$$

where $\underline{X}'_{j(1x[k+1])} = \{1, X_{1j}, X_{2j}, \ldots, X_{kj}\}$ and $\underline{\gamma}'_{j(1x[k+1])} = \{\sum_{i=1}^{k} \beta_i u_{ij}, 0, 0, \ldots, 0\}$. Thus $\underline{\gamma}_j$ can be thought of as $\underline{\beta}_j$ - $\underline{\beta}$ with $\underline{\gamma}_j \sim N_{k+1}(\underline{0}, \Sigma)$. In the case of a first order model with independent ME among the factors (i.e., $E(u_i, u_{i'}) = 0 \ \forall$ i, i ≠ i'), Σ is a matrix of zeroes aside from the [1,1] element, which is $\sum_{i=1}^{k} \beta_i^2 \sigma_i^2$.

The analysis of random coefficient models can be performed utilizing Iteratively Weighted Least Squares (IRWLS) analysis when an estimate of the ME variance is available. However, The IRWLS analysis is usually not useful, since the ME variance is unestimable from a data set containing Berkson error (Carroll, Ruppert, and Stefanski, 1995). When the value of $\sigma_i^2$ (i=1,2,…,k) is unknown , a secondary source is required to adequately estimate the ME variance. In the case of a first order model, the OLS analysis yields unbiased estimates for the model coefficients.

### 4.1.2 Second Order Models

Second order models with Berkson error do not fit the format of random coefficient models, because the intercept is no longer unbiased, i.e., the $E(\underline{\gamma}_j) \neq \underline{0}$. The models require an IRWLS procedure for analysis. The development of this analysis for the second order model follows.

Consider the Generalized Least Squares (GLS) approach to estimating the coefficients of a second order model with k design factors (regressors) in which all k factors involve Berkson error:

$$y_i = \beta_0 + \sum_{j=1}^{k} \beta_j x_{ji} + \sum_{j=1}^{k-1} \sum_{m>j}^{k} \beta_{jm}\, x_{ji}\, x_{mi} + \sum_{j=1}^{k} \beta_{jj} x_{ji}^{\,2} + e_i$$

$$= \underline{X}_i{}'\underline{\beta} + \sum_{j=1}^{k} \beta_{jj}\sigma_j^{\,2} + \varepsilon_i, \text{ where}$$

$$\varepsilon_i = e_i + \sum_{j=1}^{k} (\beta_j u_{ji} + 2\beta_{jj} X_{ji} u_{ji} + \beta_{jj}\,(u_{ji}^{\,2} - \sigma_j^{\,2})) + \sum_{j=1}^{k-1} \sum_{m>j}^{k} \beta_{jm} X_{mi} u_{ji}.$$

The GLS estimates are those which minimize

$$L = (\underline{y} - \underline{\mu})' V^{-1} (\underline{y} - \underline{\mu}),$$

where $\underline{\mu} = E[\underline{y}]$ and V is the covariance matrix for $\underline{y}$. The mean response ($E[y_i]$) is now a function of the ME variances, $\sigma_i^2$, as well as the design levels and the unknown parameters $\underline{\beta}$. In this situation $\underline{\mu}$ is a vector whose i$^{th}$ component is

$$\mu_i = \underline{X}_i{}'\underline{\beta} + \sum_{j=1}^{k} \beta_{jj}\sigma_j^{\,2} = \underline{X}_i{}^{*}{}'\underline{\beta}, \text{ where}$$

$$\underline{X}_i{}^{*}{}' = \underline{X}_i{}' + \{\ \underline{0}'_{1\text{x}\,q}, \sigma_1^{\,2}, \sigma_2^{\,2}, \ldots, \sigma_k^{\,2}\ \}.$$

The model matrix of interest is then redefined to be X*. Note that $q = 1 + k + \binom{k}{2}$, so that only the columns of the model matrix involving the quadratic terms of the design factors differ from the usual model matrix X. V, the covariance matrix of $\underline{y}$, is a diagonal matrix whose i$^{th}$ diagonal is

$$v_i = \sigma_0^{\,2} + \sum_{j=1}^{k} [(\beta_j + 2\beta_{jj} X_{ji} + \sum_{m>j}^{k} \beta_{jm} X_{mi})^2 \cdot \sigma_j^{\,2} + 2\beta_{jj}^{\,2}\sigma_j^{\,4}]. \qquad (4.2)$$

If V and the measurement error variances $\sigma_j^2$ ($j = 1, \ldots, k$) are assumed to be known, then the estimates for $\underline{\beta}$ are solutions to the equations

$$\partial L/\partial \underline{\beta} = 2\, \partial \underline{\mu}'/\partial \underline{\beta}\, V^{-1}\, (\underline{y} - \underline{\mu}) = X^{*\prime} V^{-1}(\underline{y} - X^{*\prime}\underline{\beta}) = \underline{0},$$

$$\text{or } \underline{b} = (X^{*\prime}V^{-1}X^{*})^{-1}X^{*\prime}V^{-1}\underline{y}.$$

Note that $E(\underline{b}) = (X^{*\prime}V^{-1}X^{*})^{-1}X^{*\prime}V^{-1}\, X^{*}\underline{\beta} = \underline{\beta}$. It follows that the asymptotic covariance matrix for $\underline{b}$ is

$$\text{var}(\underline{b}) = (X^{*\prime}V^{-1}X^{*})^{-1}, \qquad (4.3)$$

and the estimated covariance matrix is

$$\hat{\text{var}}(\underline{b}) = (X^{*\prime}\, \hat{V}^{-1}X^{*})^{-1}.$$

The estimated covariance matrix would be both asymptotic and approximate due to the inclusion of estimates for $\underline{\beta}$ in $\hat{V}^{-1}$.

It is important to notice that because

$$\underline{\hat{y}} = X'\underline{b} = X'(X^{*\prime}V^{-1}X^{*})^{-1}X^{*\prime}V^{-1}\underline{y},$$

$$\text{and thus var}(\underline{\hat{y}}) = X'(X^{*\prime}V^{-1}X^{*})^{-1}X,$$

prediction variances contain both the typical and the modified model matrix. These variances are more complicated than in a typical weighted regression setting.

### 4.1.3 A Note on Assumptions

The assumption that the ME variances are known can be a troublesome one, but it must be made in the present situation. If the analysis is to be based on the design used in the study, then the only observation of the ME variances occurs through the observation of the response. Because the ME variances are inseparable from the random variation assumed in *y* ($\sigma_0^2$), independent estimates of the ME variances need to be supplied. For example, some type of pre-study or discussion with the experimenter may yield satisfactory estimates for the $\sigma_i^2$. For the purpose of these simulation studies, the ME variance is assumed to be known.

The misspecification of these variances will be explored in the next chapter. Two approaches to misspecification will be considered. These studies will be aimed at the robustness of the estimation procedure to incorrect ME variance estimates.

## 4.2 Simulation Details

Data sets for a second order model involving ME in the design levels were simulated. These data sets were used to compare the performance of OLS and IRWLS analyses.

Observations were simulated over a range of experimental design situations. The data sets were created from a single variable second order model,

$$y_i = \beta_0 + \beta_1 x_i + \beta_{11} x_i^2 + e_i, \quad i = 1, 2, ..., n, \tag{4.4}$$
$$x_i = X_i + u_i,$$
$$e_i \sim N(0, 1),$$
$$u_i \sim N(0, \sigma_1^2),$$

where var($y_i$) is a special case of equation (1.10),

$$\text{var}(y_i) = \sigma_0^2 + \sigma_1^2 [\beta_1^2 + 4\beta_1\beta_{11}X_i + 4\beta_{11}^2 X_i^2] + 2\beta_{11}^2\sigma_1^4. \tag{4.5}$$

In order to observe an acceptable level of precision in the simulations, a random number generator was created (see Appendix D for details). To determine that all random data sets generated were normal, the first through fourth moments were calculated and found to be within a desired level of precision. Covariance between the model error and the ME error variable was also evaluated and found to be zero. To keep the variability of the variances at an acceptable level, 2000 data sets were generated for each experimental situation. Twenty-five runs using 2000 data sets showed that the simulated variances of the model error term were always within 1±0.066.

The parameters which were varied included model coefficients ($\beta_1$ and $\beta_{11}$), design size and point allocation, and the magnitude of ME as a percentage of the range of *X*. All combinations of these parameters are displayed in Table 4.1. Because the magnitude of the measurement error is dependent upon the model coefficients, values for $\beta_1$ and $\beta_{11}$ were varied over several combinations of integers between -3 and 3. The intercept remained at $\beta_0 = 1$ throughout the simulations. The magnitude of the ME in *x* was considered in relation to the range of *x*, which was 4. The standard deviation of the ME is specified as a percentage of the range. For example, consider a system containing 10% ME. A design level of -2 would take on a value in the range (-2.4, -1.6) about 68% of the time, since 10% of 4 is 0.4. The possible $\sigma_u$ values ranged from 1.25% of the range (0.05) to 10% of the range (0.40).

Since the measurement error is also dependent on the values of the design variable, various designs were considered. The data sets ranged in size from 5 to 100 points. Balanced designs were those with an equal sample size in the *X* variable at each point in the vector (-2, -1, 0, 1, 2). Four unbalanced designs were considered (see Table 4.3).

The comparisons focused on the individual variances for $b_1$ and $b_{11}$, the estimates of $\beta_1$ and $\beta_{11}$. Each data set was analyzed by the OLS "naïve" method and the correct method described in

Section 4.1.2. The goal of the comparison was to determine a point at which the two analysis methods yield practically different results. Since both methods lead to unbiased estimates of the coefficients, only the variances of these estimates were considered. Table 4.2 describes the statistics used to summarize the simulations for both $\beta_1$ and $\beta_{11}$. Each type of variance is explained, and all are used in the discussion of simulation results.

An experimenter ignoring the ME in the designed experiment would typically choose to analyze these data sets using OLS. The estimate of the variance of $\underline{b}_{OLS}$ would be

$$\hat{\mathrm{var}}(\underline{b}_{OLS}) = (X'X)^{-1} \cdot MSE.$$

Note that MSE is not an estimate of the variance of $y_i$, since the system has heterogenous variance due to ME. MSE is not an estimate of $\sigma_0^2$ either, but it yields an idea of the average var($y_i$) across the designed experiment. The inflation in the variance is a function of the design and the true coefficient values, as can be seen in equation 4.5. The true variance of the OLS estimates is

$$\mathrm{var}(\underline{b}_{OLS}) = (X'X)^{-1}X'VX(X'X)^{-1},$$

where V is the variance-covariance matrix of $\underline{y}$ described in Section 4.1.2.

The correct analysis for the simulated data sets is IRWLS, as previously noted. The IRWLS estimation procedure is based on the following relationship

$$\mu(\underline{\beta}, \underline{x}_i) \approx \mu(\underline{\beta}_{(0)}, \underline{x}_i) + \Sigma_i\, [\partial\mu(\underline{\beta}, \underline{x}_i)/\,\partial\beta_i]\cdot(\beta_i - \beta_{i,(0)}),$$

which is a first order Taylor Series expansion of $\mu(\underline{\beta}, \underline{x}_i)$ around $\underline{\beta} = \underline{\beta}_{(0)}$, the initial estimates for the model coefficients. In the presence of ME, IRWLS estimates are produced by the following algorithm: (1) OLS analysis is used to produce initial estimates for $\underline{\beta}_{(0)}$ and $\underline{\hat{y}}_0$. (2) The initial estimates are used to estimate

$$\underline{\hat{\gamma}}_0 = (X^{*\prime}V^{-1}X^*)^{-1}X^{*\prime}V^{-1}(\underline{y} - \underline{\hat{y}}_0),$$

where the diagonal values for V are

$$v_{ii} = MSE_0 + \sigma_1^2\,[b_{1(0)}^{\ 2} + 4b_{1(0)}b_{11(0)}X_i + 4b_{11(0)}^{\ 2}X_i^2] + 2b_{11(0)}^{\ 2}\sigma_1^4. \qquad (4.6)$$

(3) An updated estimate for the model coefficients is computed as $\underline{b}_{(1)} = \underline{b}_{(0)} + \underline{\hat{\gamma}}_0$. (4) Steps (2) - (3) are repeated until the difference in the residual sum of squares from the final step and the preceding step is less than $10^{-8}$. The estimates for $\underline{\beta}$ produced in the final iteration are the IRWLS estimates.

Because of the asymptotic properties of the covariance matrix for $\underline{\beta}$ in an IRWLS analysis, the simulation also provided a idea of the sample size for which the matrix effectively represents the true variance of the system. After the initial sample size study, further investigations into design impact and the effect of ME magnitude were explored using a sufficiently large design (see Section 4.3.1).

Table 4.1 Simulation Parameters

| Parameter | Values used in Simulation Results |
|---|---|
| $\beta_1$ * | -3, -1, 1, 3 |
| $\beta_{11}$ * | -3, -1, 1, 3 |
| ME (as percentage of *x* range) | 1.25, 2.5, 5, 7.5, 10 |
| Balanced Design Levels** | -2, -1, 0, 1, 2 |
| Balanced Design Size: n ($n_i$) | 5 (1), 10 (2), 25 (5), 50 (10), 100 (20) |

*All possible combinations of $\beta_1$ and $\beta_{11}$ were used.

**See Table 4.3 for other designs.

Table 4.2 Types of Variance Calculations for Simulated Analysis Comparisons

| Variance Type | Calculation | Use |
|---|---|---|
| IRWLS Variance | $\dfrac{\sum_{i=1}^{2000}(\hat{\beta}_{\mathrm{IRWLS}i}-\bar{\hat{\beta}})^2}{1999}$ | to compare the two analysis methods |
| OLS Variance | $\dfrac{\sum_{i=1}^{2000}(\hat{\beta}_{\mathrm{OLS}\,i}-\bar{\hat{\beta}})^2}{1999}$ | same as above |
| Asymptotic IRWLS Variance | diagonal values of $(X^{*\prime}V^{-1}X^{*})^{-1}$ | to validate the simulation and check asymptotic results for the IRWLS procedure |
| Asymptotic OLS Variance | diagonal values of $(X'X)^{-1}X'VX(X'X)^{-1}$ | to validate the simulation |
| IRWLS AEV (average estimated variance) | average diagonal values of $(X^{*\prime}\hat{V}^{-1}X^{*})^{-1}$ | to compare the variance estimation capability of the two methods |
| OLS AEV (average estimated variance) | average diagonal values of $(X'X)^{-1}\cdot \mathrm{MSE}$ | same as above |

## 4.3 Simulation Results

In many of the figures included in this section, the simulation statistic is plotted against different sets of coefficients in the model. Because of the large number of combinations, the horizontal axis does not label every point included on the graph. Since the individual points represent a set of coefficients and a value representing the amount of ME in the system, a complete listing of the coefficient values appears below. This pattern is repeated for each level of ME variance.

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $\beta_1$: | -3 | -3 | -3 | -3 | -1 | -1 | -1 | -1 | 1 | 1 | 1 | 1 | 3 | 3 | 3 | 3 |
| $\beta_{11}$: | -3 | -1 | 1 | 3 | -3 | -1 | 1 | 3 | -3 | -1 | 1 | 3 | -3 | -1 | 1 | 3 |

The following sections summarize results for the effects of sample size, the estimation of variability, the effects of ME magnitude, and the effects of design for the two analysis methods.

### 4.3.1 Sample Size

The effects of sample size were studied using balanced 5-level designs with 1 to 20 observations at each level. The simulated variances of the coefficient estimates for $\beta_1$ and $\beta_{11}$ were compared for the two analysis methods. The results (for estimation of $\beta_{11}$) for each design are plotted in Figure 4.1 and are indicated by sample size in the legend. The difference in variance is representative of data with a ME standard deviation of 10% of the range of $X_1$. Results for $\beta_1$ are similar. According to simulation results, the two analyses of data which include ME show a steadily decreasing difference in variance magnitude as the sample size increases. As expected, the IRWLS variance is almost always smaller than the OLS variance of the coefficients, but this difference decreases as sample size increases.

The greatest differences occur for large absolute values of the $\beta_{11}$ coefficient. For example, consider a 5-point design. The difference in variance for the two analysis methods is 0.21 for the true model E[y] = 1 - 3$x_1$ - 3$x_1^2$, while the difference is only 0.04 for the true model E[y] = 1 - 3$x_1$ + $x_1^2$. However, the variances themselves are much smaller for the second model than for the first. This result prompts a comparison of the differences relative to the size of the variances.

A measure of the relative difference between the analyses is calculated as

$$\text{Relative Difference} = \frac{\text{OLSVar} - \text{IRWLSVar}}{\text{IRWLSVar}} \qquad (4.7)$$

Figure 4.2 shows the relative difference in the OLS and IRWLS variances for $\beta_{11}$. There is no definite pattern in the relative difference with respect to sample size. For example, a model with ($\beta_1$, $\beta_{11}$) = (-3, -1) has a increase in the relative difference of the variances as the sample size increases. However, the results are reversed when the true model has ($\beta_1$, $\beta_{11}$) = (1, -3), so that the relative difference in the variances decreases as the sample size increases. The relative differences in Figure 4.2 are for a standard deviation of 10% of the range of $X_1$. The results indicate that the OLS variances are 5% - 28% greater than the variances of the IRWLS coefficient estimates.

Because of the conflicting results for the relative differences in the variances from the two analysis methods, there is no compelling reason to suggest a particular sample size at which the differences are irrelevant. The two methods yield differing results regardless of sample size. Notice that the true coefficient values are more relevant than sample size in the comparative performance of the two analyses. For example, consider any specific sample size in Figure 4.1.

Models which include a quadratic term with an absolute value of 3 show a greater disparity between analyses than models with $|\beta_{11}|$ =1. Another point of interest is that the plots are basically symmetric with respect to positive and negative values of the coefficients. Because of the role of the coefficients in the variance expression (see equation 4.5), this result is intuitive.

Sample size also effects the convergence of the true IRWLS variance to the asymptotic variance. As noted previously, the form of the variance based on IRWLS is an asymptotic result (see equation 4.3). To examine the convergence rate of the simulated variance to the asymptotic variance, the difference in these values is compared for each sample size. Plots of these differences across several coefficient combinations appear in Figures 4.3 and 4.4. Figure 4.3 shows these differences for $\beta_1$, and Figure 4.4 shows the differences for $\beta_{11}$. Both figures represent situations in which the ME standard deviation is 10% of the range of $X_1$. The difference between the simulated and asymptotic values decreases dramatically with an increase in sample size in the simulated situation. This is true across all coefficient combinations. A 25-point design was chosen for future comparisons, since the difference between the asymptotic and simulated variances is fairly small at this sample size. For both $\beta_1$ and $\beta_{11}$, the difference in the simulated and asymptotic variances is 0.05 or less for a sample size of 25.

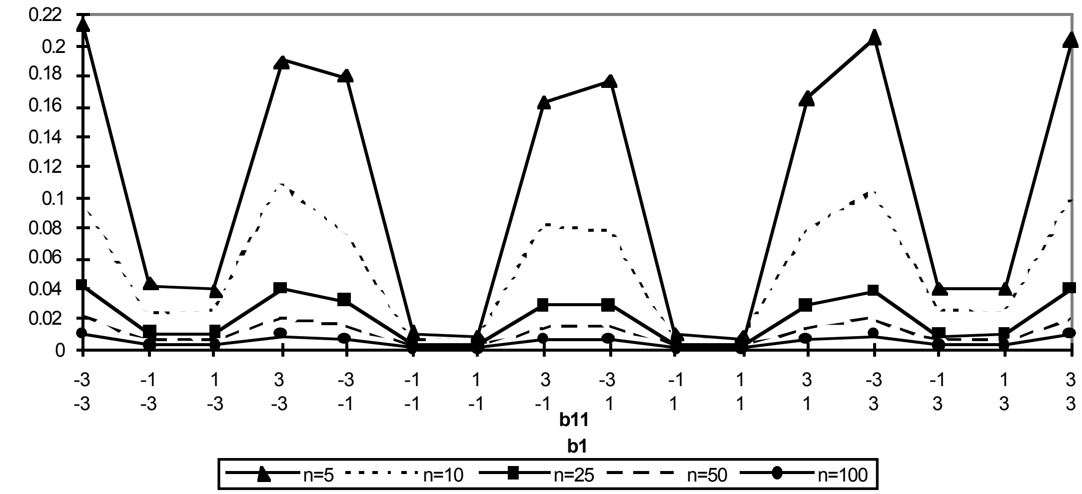


Figure 4.1 Absolute Difference in Variances of OLS and IRWLS Estimates of $\beta_{11}$ at $\sigma_u$ = 10% of the Range of $X$

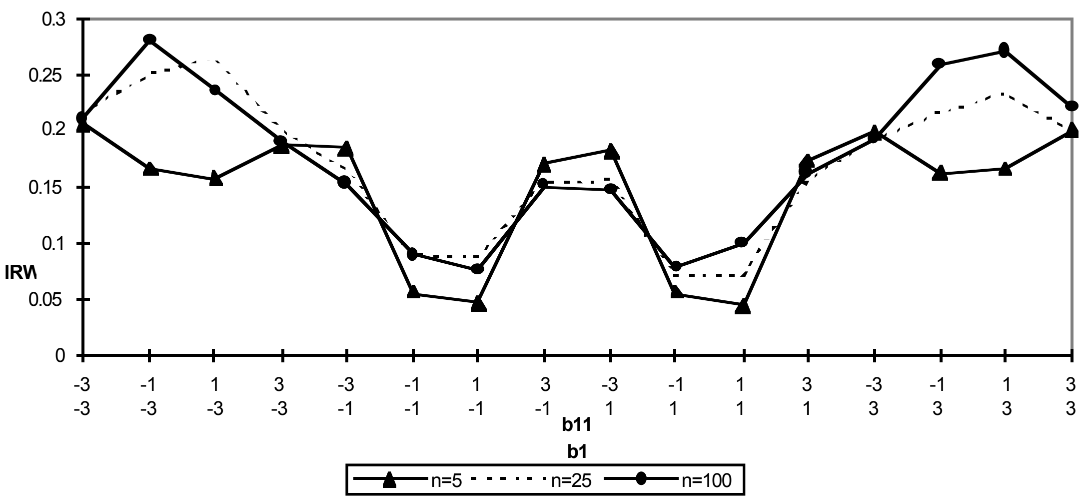


Figure 4.2 Relative Difference in Variances of OLS and IRWLS Estimates of $\beta_{11}$ at $\sigma_u$ = 10% of the Range of $X$

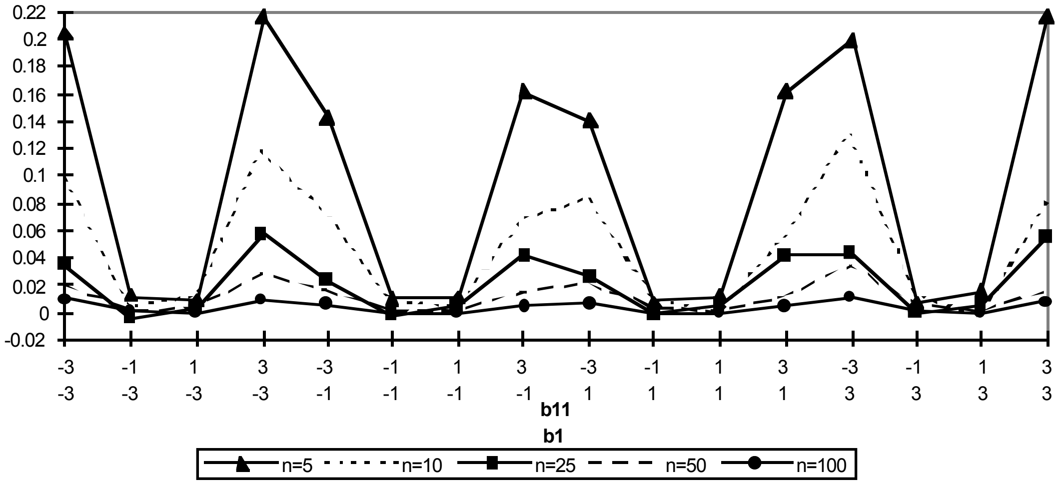


Figure 4.3 Asymptotic Results for IRWLS Estimates of $\beta_1$ when $\sigma_u$ = 10% of the Range of $X$

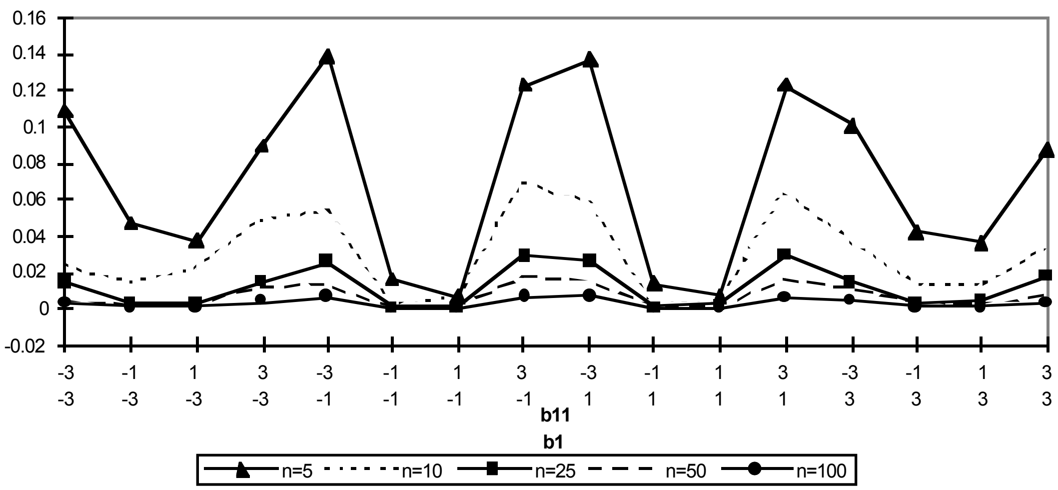


Figure 4.4 Asymptotic Results for IRWLS Estimates of $\beta_{11}$ when $\sigma_u$ = 10% of the Range of $X$

### 4.3.2 Variance Estimates in the Presence of ME

Another consideration of the simulation concerned the variance estimates for individual data sets. A comparison of each variance estimate to the corresponding simulated variance was performed. The estimated variances were calculated for both OLS and IRWLS coefficients for each of the 2000 simulated data sets, and an average estimated variance (AEV) was calculated (see Table 4.2). The average estimated variances were then compared to the simulated variance of the corresponding coefficient. The results appear in Figure 4.5 and Figure 4.6 for a 25-point design.

The variance for the OLS estimates is uniformly underestimated, while the variance for IRWLS estimates is consistently overestimated. This relationship holds true regardless of the coefficient values or the relative performance of the two analyses based on the simulated variances. This result is unfavorable for the use of either analysis, although the difference in average estimated and true variances is less of a problem for the OLS analysis. Other simulations for smaller sample sizes indicated that the disparity between the average estimates and the simulated variances increases as the sample size decreases. As a result, the situations in which the IRWLS estimates appear to have the greatest advantage over OLS analysis ( i.e., small designs) are also the situations in which the variance estimates of the IRWLS analysis are poorest.

One cause of the overestimation of IRWLS AEVs could be the initial estimates used in the weights for the analysis (see equation 4.6). The MSE from the OLS procedure is an inflated estimate of $\sigma_0^2$, but it is the most reasonable initial estimate available.

### 4.3.3 Effect of ME Magnitude

The results reported to this point have considered a ME standard deviation equal to 10% of the range of $X_1$. To evaluate the effect of the ME magnitude on the performance of the two analysis methods, several different values were considered for the ME standard deviation (see Table 4.1). The simulation results pertaining to ME magnitude demonstrate a steady increase in the absolute difference in the coefficient variances for the two analysis methods as ME magnitude increases. This result is expected. In addition, the relative difference (see equation 4.7) increases steadily. Figure 4.7 demonstrates this increase for both $\beta_1$ and $\beta_{11}$ for a 25-point balanced design.

There is no jump in the effect of ME magnitude on these analyses, so the researcher can decide on the advantage of the IRWLS analysis based upon a combination of ME magnitude, suspected magnitude of coefficients, and the available sample size for the experiment. Figure 4.7 indicates that for the given design and certain coefficient combinations, a ME magnitude as small as 5% of the range of $X$ may cause the variance in the OLS estimates to be 12% to 15% greater than the variance of the IRWLS estimates. A ME magnitude of 10% of the range leads to OLS estimates that may be 20-25% greater than IRWLS estimates. Notice again that the effect of the measurement error is directly related to the magnitude of $\beta_{11}$.

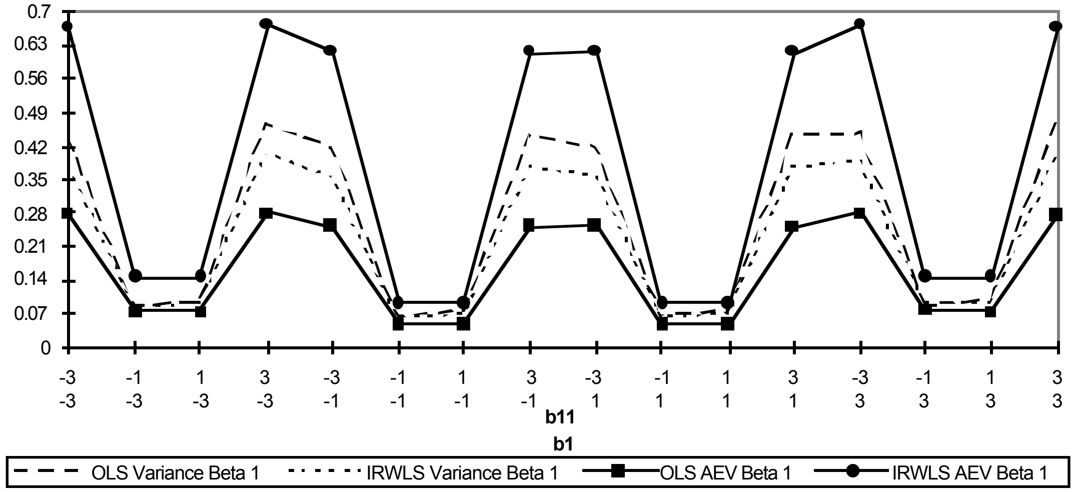


Figure 4.5 Simulated vs. Average Estimated Variance for Estimates of $\beta_1$

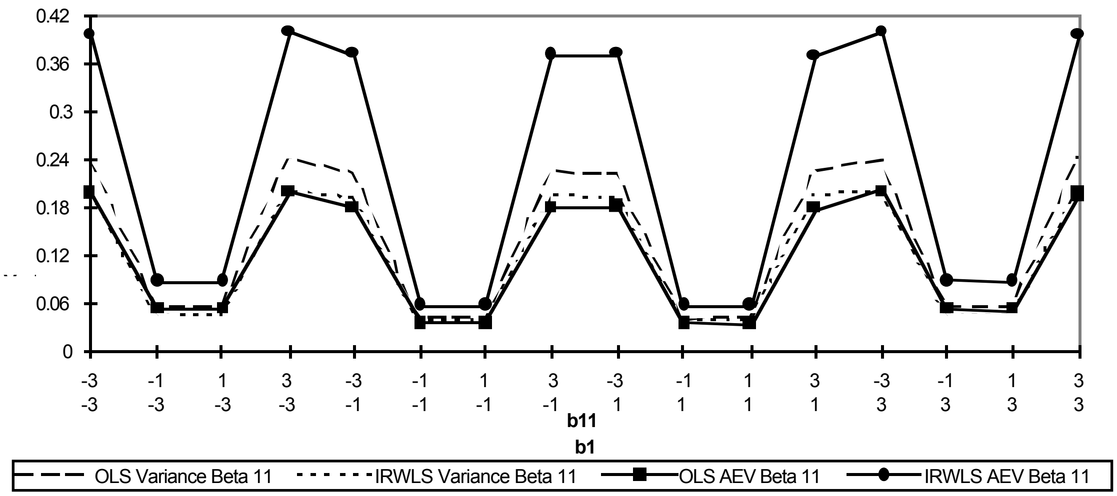


Figure 4.6 Simulated Variance vs. Average Estimated Variance for Estimates of $\beta_{11}$

### 4.3.4 Effect of Design in the Presence of ME

Recall that the previous results have been based on a design which is nicely balanced around zero. To study the effect of design on the performance of the two analyses, the balanced design was compared to other designs which are not so ideal. Each of these designs contains 25 points. The designs are listed in Table 4.3. Design 1 is the balanced design considered in previous evaluations. Designs 2 and 3 contain points placed asymmetrically around the center of the design space, so that the odd design moments for these designs are not zero. Design 4 is balanced around the design center but contains a larger percentage of center runs than Design 1.

The variance of the coefficients were compared for the four designs, and the results for $\beta_1$ and $\beta_{11}$ for each of the four designs are shown in Figures 4.7 - 4.10. The figures show the relative differences in the variance of the estimates for a grid of coefficients and a range of ME magnitude. The comparison indicates that the position of the design points is critical in determining the effect of ME on the variance of coefficient estimates, even when the design differs very little from the balanced design. For Design 1, the OLS variance for a coefficient is never more than 27% more than the IRWLS variance. However, the OLS variances for Designs 3 and 4 are 60-70% greater than the IRWLS variances in some cases. Results for Design 2 were similar to results for Design 1.

Table 4.3 Sample Sizes for Different Unbalanced Designs

| Design Levels | Design 1 ($n_i$) | Design 2 ($n_i$) | Design 3 ($n_i$) | Design 4 ($n_i$) |
|---|---|---|---|---|
| -2 | 5 | 9 | 0 | 4 |
| -1 | 5 | 4 | 9 | 4 |
| 0 | 5 | 4 | 4 | 9 |
| 1 | 5 | 4 | 4 | 4 |
| 2 | 5 | 4 | 4 | 4 |
| 3 | 0 | 0 | 4 | 0 |

Figure 4.11 and Figure 4.12 show the differences in the IRWLS variance of $\beta_1$ and $\beta_{11}$ for the three designs. Notice that the IRWLS variances are generally larger for the unbalanced designs. Investigations into designs with smaller sample sizes show an even greater discrepancy between the performances of the designs. Intuitively, a balanced design will increase the efficiency of the estimation of coefficients. The comparison of OLS and IRWLS analyses shows that a balanced design improves the efficiency of the OLS procedure even more than it improves the efficiency of

the IRWLS analysis. Of course, this also means that the IRWLS analysis is more robust to changes in design than the OLS analysis.

## 4.4 Conclusions

ME in single factor design can significantly degrade the performance of OLS analysis in comparison to IRWLS analysis. Even for a balanced design, the coefficient variances may be inflated by as much as 25%. This percentage may increase to as much as 60-65% when a less ideal design is used. These results are for 25-point designs, and ME has an even larger impact on smaller designs. At a ME magnitude of 10% of the range of the design variable, it is preferable to use the IRWLS analysis.

However, there are a few reasons for caution when using the IRWLS analysis. The estimated variances for the coefficients are inflated, which weakens resulting significance testing. Also, these results are based on a range of true coefficient values for the model. In some cases, the ME has little effect on the results of the iterative procedure. The coefficients in this example were fairly small ($|\beta_i/\sigma_0| \leq 3$), so this result may not be typical for real experiments. This is especially true of designs for second order models, which are usually needed after significant design factors have been identified in a screening experiment.

In general, the results of this chapter indicate that OLS analysis is fairly robust to ME in the design factors when a balanced design is used. However, some increase in efficiency is possible through the IRWLS analysis.

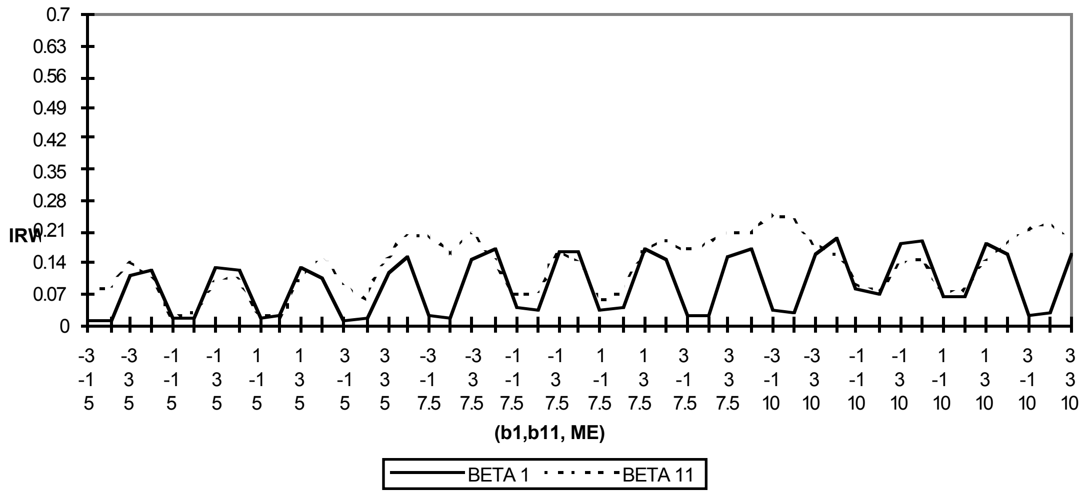


Figure 4.7 Relative Difference Between Variances of OLS and IRWLS Analyses for $\beta_1$ and $\beta_{11}$ --- Design 1

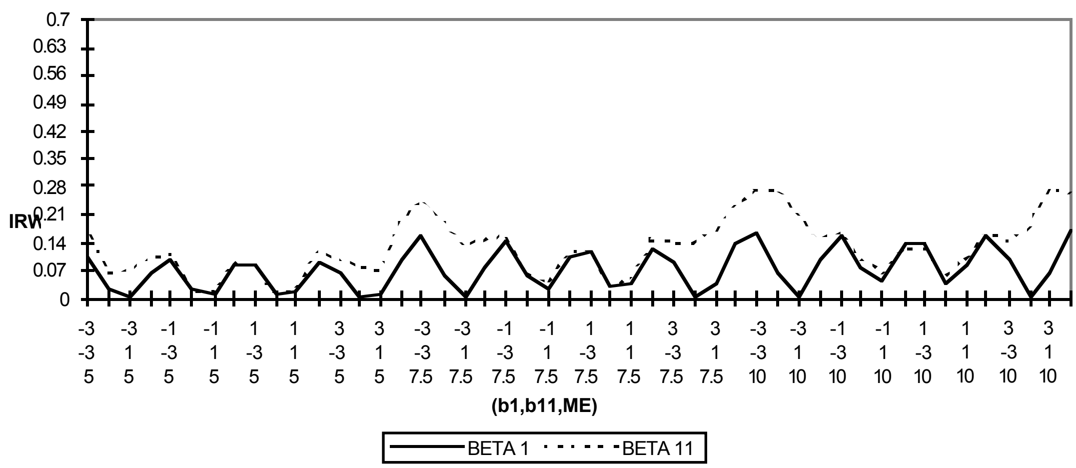


Figure 4.8 Relative Difference Between Variances of OLS and IRWLS Analyses for $\beta_1$ and $\beta_{11}$ --- Design 2

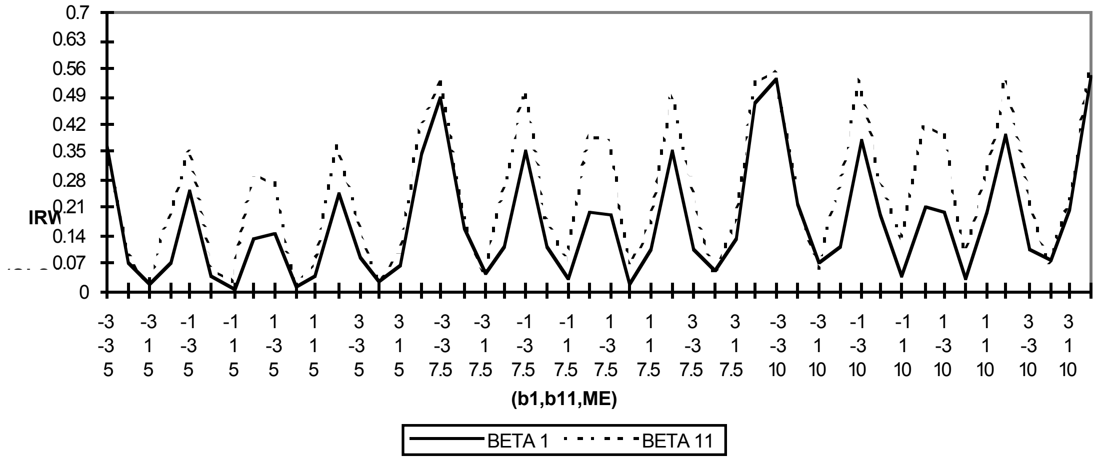


Figure 4.9 Relative Difference Between Variances of OLS and IRWLS Analyses for $\beta_1$ and $\beta_{11}$ --- Design 3

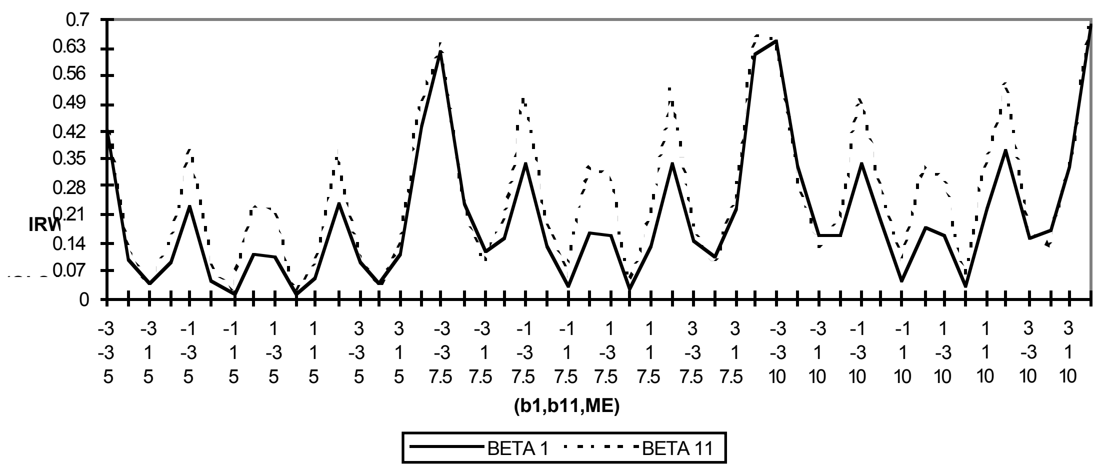


Figure 4.10 Relative Difference Between Variances of OLS and IRWLS Analyses for $\beta_1$ and $\beta_{11}$ --- Design 4

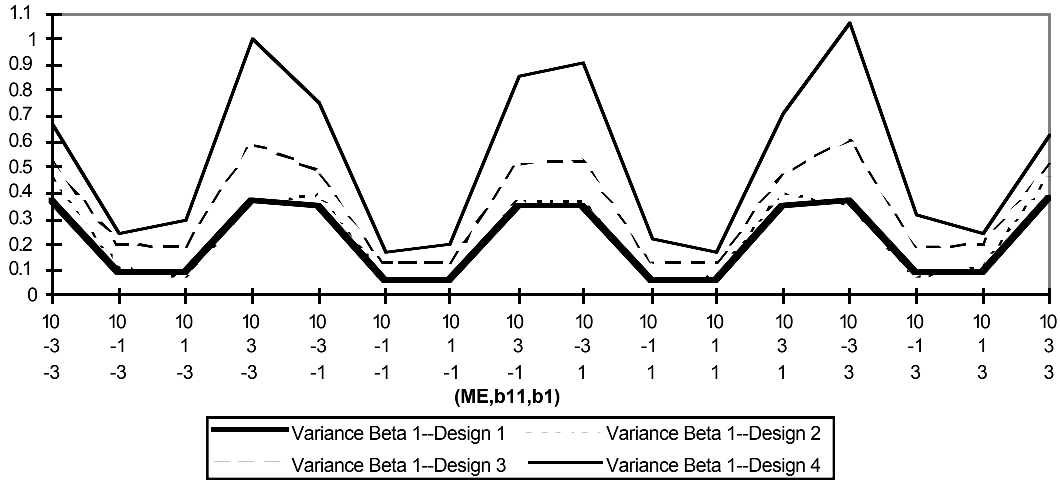


Figure 4.11 IRWLS Var of $\beta_1$ for Different Designs

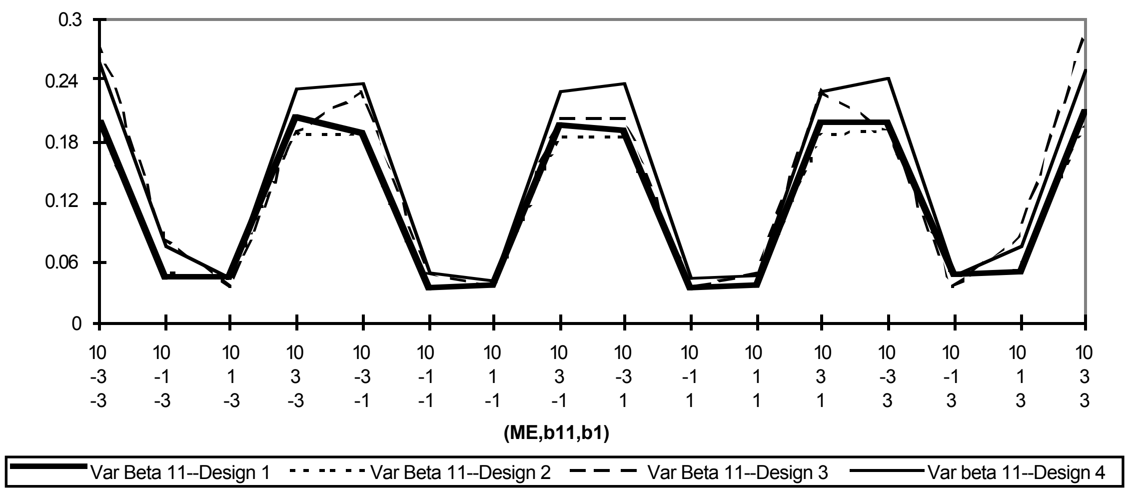


Figure 4.12 IRWLS Var of $\beta_{11}$ for Different Designs

# 5. Robustness of Analysis to ME Variance Misspecification

As stated in the previous chapter, the assumption that the ME variances are known is unrealistic in many cases. Unfortunately, the analysis of designed experiments containing ME requires an estimate of the ME variance for the estimation of the model coefficients. The ME variance estimate must be independent of the data for the designed experiment, because the variation in the design factor is indistinguishable from the variation in the response. Estimation procedures for ME variance are not an immediate question in this research. However, the robustness of the IRWLS estimation procedure to misspecification of the ME variance is of interest to experimenters accustomed to "guesstimates" of the ME variance in a particular situation. Two possibilities for ME variance misspecification are explored in this chapter: the first considers the effect of underestimating the ME variance, and the second focuses on the overestimation of the ME variance. A comparison of the performance of the IRWLS analysis in relation to the OLS analysis is summarized and presented. All robustness issues are explored for the single variable second order model presented in the previous chapter.

## 5.1 Underestimating the ME variance

Suppose the experimenter gives an estimate of the ME variance in a factor which is less than the actual variance within that design factor, $\sigma_1^2$. The estimation of the model coefficients is affected through the covariance matrix of $\underline{y}$,

$$V = \mathrm{diag}[\mathrm{var}(y_i)] = \mathrm{diag}[\sigma_0^2 + \boldsymbol{\sigma_1^2}[\beta_1^2 + 4\beta_1\beta_{11}X_i + 4\beta_{11}^2X_i^2] + 2\beta_{11}^2\boldsymbol{\sigma_1^4}],$$

and the modified model matrix

$$X^* = X + \{\underline{0}_{n \times 1}, \underline{0}_{n \times 1}, \boldsymbol{\sigma_1^2} \cdot \underline{1}_{n \times 1}\}.$$

Let $V_u$ and $X_u^*$ denote the covariance matrix for $\underline{y}$ and the modified model matrix when the estimate of the ME variance is too small. The estimates for $\underline{\beta}$ using IRWLS are no longer unbiased, since

$$E(\underline{b}_u) = (X_u^{*\prime}V_u^{-1}X_u^*)^{-1}X_u^{*\prime}V_u^{-1}X^*\underline{\beta} \neq \underline{\beta}, \qquad (5.1)$$

so that

$$\mathrm{Bias}(\underline{b}_u) = [(X^{*\prime}V^{-1}X^*)^{-1}X^{*\prime}V^{-1} - (X_u^{*\prime}V_u^{-1}X_u^*)^{-1}X_u^{*\prime}V_u^{-1}]X^*\underline{\beta}. \qquad (5.2)$$

The covariance matrix of the coefficients is also affected and is now expressed as

$$\mathrm{Var}(\underline{b}_u) = (X_u^{*\prime}V_u^{-1}X_u^*)^{-1}\, X_u^{*\prime}V^{-1}X_u^*(X_u^{*\prime}V_u^{-1}X_u^*)^{-1}. \qquad (5.3)$$

These expressions for expectation and variance of the coefficient estimates indicate that a mean-squared-error (MSE) calculation is needed for the exploration of the robustness of IRWLS analysis to ME variance misspecification. When the ME variance is underestimated, the MSE for a particular model coefficient *j* is

$$\mathrm{MSE}(b_{ju}) = \mathrm{Var}(b_{ju}) + (\mathrm{Bias}(b_{ju}))^2.$$

A relative efficiency can be calculated to compare the IRWLS and OLS analysis methods as follows:

$$RE_u = \mathrm{MSE}(b_{ju})/\mathrm{Var}(b_{jols}).$$

## 5.2 Overestimating the ME variance

An experimenter who uses an overestimate of the ME variance faces a problem similar to the case in which the ME variance is underestimated. A MSE measure of variability is required for the overestimated coefficients, $\underline{b}_o$, and a relative efficiency can again be calculated to compare the two analysis approaches for a single model coefficient. The relative efficiency is calculated as

$$RE_o = \mathrm{MSE}(b_{jo})/\mathrm{Var}(b_{jols}).$$

## 5.3 Simulation Details

For the single factor design, several degrees of ME variance underestimation were simulated. The balanced design presented in the previous chapter is used for the robustness comparisons (see Table 4.1). The design size is n = 25, so that all five design points are repeated five times. The range of the design factor is 4, since design levels are between -2 and 2. As in the previous chapter, results are stated for a range of ME standard deviation values. ME standard deviation is specified as a percentage of the range. The amount of misspecification is varied as well as the magnitude of the true ME variance. The data were analyzed using both OLS and IRWLS analyses.

Table 5.1 - Table 5.4 list relative efficiencies for situations in which the ME variance is underspecified. The first column in each table indicates the true magnitude of ME in the system, while the second column indicates the amount specified in the weights for the IRWLS analysis. The efficiencies are calculated over a grid of coefficient combinations which are listed in the first row of each table. Table 5.1 and Table 5.2 contain efficiencies for estimation of $\beta_1$, while Table 5.3 and Table 5.4 contain efficiencies for $\beta_{11}$.

Table 5.5 and 5.6 summarize the relative efficiencies for the two analyses when the ME magnitude is overspecified. The layout for these tables is similar to the tables mentioned previously. Table 5.5 contains relative efficiencies for estimation of $\beta_1$ and Table 5.6 summarizes the relative efficiencies for $\beta_{11}$.

## 5.4 Simulation Results

### 5.4.1 Underspecified ME Magnitude

Results in Tables 5.1 - 5.4 show that, regardless of the ME magnitude or the amount of underspecification of this magnitude, the IRWLS analyses are always more efficient than the OLS analyses for estimation of $\beta_1$ and $\beta_{11}$. This is very encouraging, for although the efficiency gained by using the IRWLS analysis is sometimes very slight, there are no cases where the OLS analysis actually outperforms the IRWLS analysis. The efficiencies in Tables 5.1 - 5.4 are never above 1, although in some cases the efficiency of the two analysis methods is virtually identical. Thus the IRWLS analysis is still a “safe” method of coefficient estimation, even when the ME standard deviation may be underspecified.

It is true, however, that the performance of the IRWLS analysis suffers in comparison to the OLS analysis. In other words, the improvement in estimation gained by using the IRWLS procedure decreases when the estimate for the ME variance is less than the true ME variance. For example, when the true ME standard deviation is 10% of the range of *X*, but the specified ME standard deviation is only 5% of the range of *X*, the OLS analysis is 91 - 98% efficient relative to the IRWLS analysis. When the specified ME variance is on target at 10%, the OLS analysis is only 80 - 96% efficient relative to the IRWLS analysis. These relative efficiencies can be found in Table 5.1 and Table 5.3.

However, the disparity in the relative efficiencies decreases as the true magnitude of the ME increases. Notice that when the true ME standard deviation is 25% of the range of *X*, the loss of efficiency for the IRWLS analysis is only about 2% for $\beta_1$ and a little less than 4% for $\beta_{11}$ when the ME standard deviation is underspecified at 17.5% of the range. For example, when the ME standard deviation is correctly specified and ($\beta_1$, $\beta_{11}$) = (-1,-3), the relative efficiency for estimating $\beta_1$ is 88%. This efficiency increases to 90% when the ME is specified to be 17.5% (when the true ME standard deviation is 25%). This is true across the range of coefficients in the study as is evidenced in the last row of Table 5.2 for $\beta_1$ and Table 5.4 for $\beta_{11}$.

Based on these results, the correct specification of ME seems very important to the relative performance of the IRWLS analysis. The efficiency of the OLS analysis relative to the IRWLS analysis always increases if the ME magnitude is underspecified. However, the results discussed in the following section are more encouraging.

### 5.4.2 Overspecified ME Magnitude

When the magnitude of ME is overspecified, the performance of the IRWLS analysis is often enhanced. The efficiency of the OLS analysis relative to the IRWLS analysis decreases in many situations. This is true across the board for ME standard deviations which are greater than 7.5% of the range of *X*, even when the specified ME standard deviation is almost double that of the true magnitude. The few exception occur when the magnitude of the ME is small in relation to the range of *X* (5% or less). In these cases, the difference between the analysis methods is negligible from the start.

Overspecifying the ME variance seems preferable in some cases where the true ME magnitude is small, but these situations are dependent upon the true coefficient values. For example, consider a true ME standard deviation of 5% of the range. The relative efficiency of OLS analysis decreases for coefficients ($\beta_1$, $\beta_{11}$) = (-1, -3), but the relative efficiency increases for coefficients (-1, -1). This is evident for the estimation of both $\beta_1$ (see Table 5.5) and $\beta_{11}$ (see Table 5.6)

## 5.5 Conclusions

Misspecification of the ME variance does affect the performance of the IRWLS analysis. When the specified variance is less than the true magnitude of the ME variance in the system, the performance of the IRWLS analysis suffers in comparison to the OLS analysis. However, when the specified ME variance is greater than the true ME variance, the performance of the IRWLS analysis often improves. This is especially true when the standard deviation of the ME is 7.5% of the range of *X* or more. In the cases where the standard deviation of the ME is 5% of the range of *X* or less, the IRWLS analysis offers only a slight improvement over the OLS analysis anyway. Based on these results, it seems beneficial for the experimenter to be conservative when specifying the ME variance and use a value that is too large rather than too small.

Table 5.1 Relative Efficiencies for OLS vs. IRWLS [ME is Underspecified--$\beta_1$]

| $\beta_1$ | | -3 | -3 | -3 | -1 | -1 | -1 | -1 | 1 | 1 | 1 | 1 | 3 | 3 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $\beta_{11}$ | | -3 | -1 | 3 | -3 | -1 | 1 | 3 | -3 | -1 | 1 | 3 | -3 | 3 |
| True ME | Spec ME | | | | | | | | | | | | | |
| 5.0 | 5.0 | 0.90 | 0.99 | 0.90 | 0.89 | 0.98 | 0.98 | 0.89 | 0.89 | 0.99 | 0.98 | 0.88 | 0.90 | 0.89 |
| 5.0 | 2.5 | 0.95 | 0.99 | 0.95 | 0.94 | 0.99 | 0.99 | 0.95 | 0.94 | 0.99 | 0.99 | 0.95 | 0.95 | 0.96 |
| | | | | | | | | | | | | | | |
| 6.25 | 6.25 | 0.86 | 0.98 | 0.88 | 0.85 | 0.96 | 0.97 | 0.87 | 0.86 | 0.97 | 0.98 | 0.87 | 0.88 | 0.88 |
| 6.25 | 1.25 | 0.99 | 0.99 | 0.99 | 0.99 | 0.99 | 0.99 | 0.99 | 0.99 | 0.99 | 0.99 | 0.99 | 0.99 | 0.99 |
| | | | | | | | | | | | | | | |
| 7.5 | 7.5 | 0.87 | 0.98 | 0.87 | 0.85 | 0.96 | 0.97 | 0.86 | 0.85 | 0.96 | 0.96 | 0.85 | 0.87 | 0.86 |
| 7.5 | 5.0 | 0.92 | 0.98 | 0.92 | 0.91 | 0.97 | 0.97 | 0.91 | 0.91 | 0.97 | 0.97 | 0.91 | 0.92 | 0.92 |
| 7.5 | 2.5 | 0.97 | 0.99 | 0.97 | 0.97 | 0.99 | 0.99 | 0.97 | 0.97 | 0.99 | 0.99 | 0.97 | 0.97 | 0.97 |
| | | | | | | | | | | | | | | |
| 10.0 | 10.0 | 0.85 | 0.96 | 0.86 | 0.84 | 0.93 | 0.94 | 0.84 | 0.84 | 0.94 | 0.94 | 0.84 | 0.86 | 0.86 |
| 10.0 | 7.5 | 0.90 | 0.98 | 0.90 | 0.88 | 0.95 | 0.95 | 0.89 | 0.89 | 0.95 | 0.95 | 0.88 | 0.90 | 0.90 |
| 10.0 | 5.0 | 0.94 | 0.98 | 0.94 | 0.93 | 0.97 | 0.97 | 0.93 | 0.93 | 0.97 | 0.97 | 0.93 | 0.94 | 0.94 |
| 10.0 | 2.5 | 0.98 | 0.99 | 0.98 | 0.97 | 0.99 | 0.99 | 0.98 | 0.98 | 0.99 | 0.99 | 0.98 | 0.98 | 0.98 |
| | | | | | | | | | | | | | | |
| 12.5 | 12.5 | 0.86 | 0.96 | 0.86 | 0.85 | 0.92 | 0.92 | 0.85 | 0.85 | 0.92 | 0.92 | 0.85 | 0.87 | 0.86 |
| 12.5 | 10.0 | 0.88 | 0.97 | 0.89 | 0.87 | 0.93 | 0.93 | 0.87 | 0.87 | 0.93 | 0.93 | 0.87 | 0.89 | 0.88 |
| 12.5 | 7.5 | 0.92 | 0.98 | 0.92 | 0.90 | 0.95 | 0.95 | 0.91 | 0.91 | 0.95 | 0.95 | 0.90 | 0.92 | 0.92 |
| 12.5 | 5.0 | 0.95 | 0.99 | 0.96 | 0.95 | 0.97 | 0.97 | 0.95 | 0.95 | 0.97 | 0.97 | 0.95 | 0.96 | 0.95 |

Table 5.2 Relative Efficiencies for OLS vs. IRWLS Analyses When ME is Underspecified ($\beta_1$)

| $\beta_1$ | | -3 | -3 | -3 | -1 | -1 | -1 | -1 | 1 | 1 | 1 | 1 | 3 | 3 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $\beta_{11}$ | | -3 | -1 | 3 | -3 | -1 | 1 | 3 | -3 | -1 | 1 | 3 | -3 | 3 |
| True ME | Spec ME | | | | | | | | | | | | | |
| 15.0 | 15.0 | 0.86 | 0.95 | 0.86 | 0.85 | 0.90 | 0.91 | 0.85 | 0.85 | 0.90 | 0.90 | 0.85 | 0.86 | 0.86 |
| 15.0 | 12.5 | 0.88 | 0.96 | 0.88 | 0.86 | 0.91 | 0.92 | 0.87 | 0.87 | 0.92 | 0.92 | 0.87 | 0.89 | 0.88 |
| 15.0 | 10.0 | 0.90 | 0.97 | 0.91 | 0.89 | 0.93 | 0.94 | 0.89 | 0.89 | 0.94 | 0.94 | 0.89 | 0.91 | 0.91 |
| 15.0 | 7.5 | 0.93 | 0.98 | 0.94 | 0.93 | 0.95 | 0.96 | 0.93 | 0.93 | 0.96 | 0.95 | 0.93 | 0.94 | 0.94 |
| | | | | | | | | | | | | | | |
| 17.5 | 17.5 | 0.86 | 0.95 | 0.87 | 0.85 | 0.90 | 0.90 | 0.86 | 0.86 | 0.91 | 0.90 | 0.85 | 0.87 | 0.87 |
| 17.5 | 15.0 | 0.88 | 0.96 | 0.88 | 0.87 | 0.91 | 0.91 | 0.87 | 0.87 | 0.91 | 0.91 | 0.87 | 0.88 | 0.88 |
| 17.5 | 10.0 | 0.92 | 0.98 | 0.92 | 0.91 | 0.94 | 0.94 | 0.91 | 0.91 | 0.94 | 0.94 | 0.91 | 0.92 | 0.92 |
| | | | | | | | | | | | | | | |
| 20.0 | 20.0 | 0.87 | 0.95 | 0.88 | 0.86 | 0.89 | 0.91 | 0.87 | 0.86 | 0.90 | 0.90 | 0.87 | 0.88 | 0.88 |
| 20.0 | 17.5 | 0.88 | 0.96 | 0.89 | 0.87 | 0.90 | 0.91 | 0.88 | 0.87 | 0.90 | 0.91 | 0.88 | 0.89 | 0.89 |
| 20.0 | 15.0 | 0.89 | 0.96 | 0.90 | 0.88 | 0.91 | 0.92 | 0.89 | 0.88 | 0.92 | 0.91 | 0.89 | 0.90 | 0.89 |
| 20.0 | 12.5 | 0.91 | 0.96 | 0.91 | 0.90 | 0.92 | 0.93 | 0.90 | 0.90 | 0.93 | 0.94 | 0.90 | 0.91 | 0.91 |
| | | | | | | | | | | | | | | |
| 22.5 | 22.5 | 0.88 | 0.95 | 0.89 | 0.86 | 0.90 | 0.90 | 0.86 | 0.87 | 0.90 | 0.89 | 0.86 | 0.88 | 0.87 |
| 22.5 | 20.0 | 0.89 | 0.96 | 0.89 | 0.88 | 0.90 | 0.91 | 0.88 | 0.87 | 0.90 | 0.91 | 0.88 | 0.88 | 0.89 |
| 22.5 | 15.0 | 0.91 | 0.96 | 0.91 | 0.90 | 0.92 | 0.93 | 0.90 | 0.90 | 0.93 | 0.93 | 0.90 | 0.92 | 0.91 |
| | | | | | | | | | | | | | | |
| 25.0 | 25.0 | 0.89 | 0.94 | 0.89 | 0.88 | 0.90 | 0.90 | 0.88 | 0.88 | 0.90 | 0.90 | 0.88 | 0.89 | 0.89 |
| 25.0 | 22.5 | 0.88 | 0.95 | 0.88 | 0.87 | 0.89 | 0.90 | 0.87 | 0.87 | 0.90 | 0.91 | 0.87 | 0.88 | 0.89 |
| 25.0 | 20.0 | 0.90 | 0.96 | 0.90 | 0.89 | 0.91 | 0.92 | 0.89 | 0.89 | 0.91 | 0.91 | 0.89 | 0.90 | 0.90 |
| 25.0 | 17.5 | 0.91 | 0.96 | 0.91 | 0.90 | 0.92 | 0.92 | 0.90 | 0.90 | 0.92 | 0.92 | 0.90 | 0.91 | 0.91 |

Table 5.3 Relative Efficiencies for OLS vs. IRWLS Analyses When ME is Underspecified ($\beta_{11}$)

| $\beta_1$ | | -3 | -3 | -3 | -1 | -1 | -1 | -1 | 1 | 1 | 1 | 1 | 3 | 3 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $\beta_{11}$ | | -3 | -1 | 3 | -3 | -1 | 1 | 3 | -3 | -1 | 1 | 3 | -3 | 3 |
| True ME | Spec ME | | | | | | | | | | | | | |
| 5.0 | 5.0 | 0.87 | 0.93 | 0.88 | 0.91 | 0.99 | 0.98 | 0.91 | 0.90 | 0.98 | 0.99 | 0.91 | 0.87 | 0.87 |
| 5.0 | 2.5 | 0.93 | 0.96 | 0.93 | 0.96 | 0.99 | 0.99 | 0.96 | 0.96 | 0.99 | 0.99 | 0.96 | 0.94 | 0.94 |
| | | | | | | | | | | | | | | |
| 6.25 | 6.25 | 0.84 | 0.88 | 0.84 | 0.88 | 0.96 | 0.96 | 0.88 | 0.88 | 0.97 | 0.97 | 0.89 | 0.85 | 0.85 |
| 6.25 | 1.25 | 0.98 | 0.99 | 0.98 | 0.99 | 0.99 | 0.99 | 0.99 | 0.99 | 0.99 | 0.99 | 0.99 | 0.98 | 0.98 |
| | | | | | | | | | | | | | | |
| 7.5 | 7.5 | 0.83 | 0.83 | 0.83 | 0.87 | 0.94 | 0.94 | 0.86 | 0.88 | 0.95 | 0.93 | 0.86 | 0.84 | 0.83 |
| 7.5 | 5.0 | 0.88 | 0.89 | 0.89 | 0.92 | 0.96 | 0.96 | 0.92 | 0.92 | 0.97 | 0.97 | 0.93 | 0.89 | 0.89 |
| 7.5 | 2.5 | 0.96 | 0.96 | 0.96 | 0.97 | 0.99 | 0.99 | 0.98 | 0.97 | 0.99 | 0.99 | 0.98 | 0.96 | 0.96 |
| | | | | | | | | | | | | | | |
| 10.0 | 10.0 | 0.83 | 0.80 | 0.85 | 0.86 | 0.92 | 0.93 | 0.88 | 0.87 | 0.93 | 0.93 | 0.88 | 0.85 | 0.84 |
| 10.0 | 7.5 | 0.86 | 0.85 | 0.87 | 0.90 | 0.94 | 0.94 | 0.91 | 0.90 | 0.94 | 0.94 | 0.90 | 0.87 | 0.86 |
| 10.0 | 5.0 | 0.91 | 0.91 | 0.92 | 0.94 | 0.96 | 0.96 | 0.95 | 0.95 | 0.96 | 0.96 | 0.94 | 0.92 | 0.91 |
| 10.0 | 2.5 | 0.97 | 0.97 | 0.97 | 0.98 | 0.99 | 0.99 | 0.98 | 0.98 | 0.99 | 0.99 | 0.98 | 0.97 | 0.97 |
| | | | | | | | | | | | | | | |
| 12.5 | 12.5 | 0.82 | 0.77 | 0.83 | 0.85 | 0.88 | 0.90 | 0.86 | 0.85 | 0.90 | 0.91 | 0.86 | 0.83 | 0.83 |
| 12.5 | 10.0 | 0.85 | 0.80 | 0.85 | 0.89 | 0.91 | 0.91 | 0.89 | 0.90 | 0.92 | 0.90 | 0.89 | 0.86 | 0.85 |
| 12.5 | 7.5 | 0.89 | 0.85 | 0.89 | 0.93 | 0.93 | 0.93 | 0.92 | 0.93 | 0.94 | 0.93 | 0.92 | 0.89 | 0.89 |
| 12.5 | 5.0 | 0.93 | 0.91 | 0.94 | 0.96 | 0.96 | 0.96 | 0.96 | 0.96 | 0.96 | 0.97 | 0.96 | 0.94 | 0.94 |

Table 5.4 Relative Efficiencies for OLS vs. IRWLS [ME is Underspecified--$\beta_{11}$]

| $\beta_1$ | | -3 | -3 | -3 | -1 | -1 | -1 | -1 | 1 | 1 | 1 | 1 | 3 | 3 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $\beta_{11}$ | | -3 | -1 | 3 | -3 | -1 | 1 | 3 | -3 | -1 | 1 | 3 | -3 | 3 |
| True ME | Spec ME | | | | | | | | | | | | | |
| 15.0 | 15.0 | 0.83 | 0.75 | 0.82 | 0.87 | 0.89 | 0.88 | 0.86 | 0.87 | 0.88 | 0.88 | 0.86 | 0.82 | 0.83 |
| 15.0 | 12.5 | 0.85 | 0.79 | 0.87 | 0.89 | 0.89 | 0.91 | 0.90 | 0.90 | 0.91 | 0.91 | 0.90 | 0.87 | 0.86 |
| 15.0 | 10.0 | 0.88 | 0.83 | 0.89 | 0.91 | 0.91 | 0.93 | 0.92 | 0.93 | 0.92 | 0.93 | 0.92 | 0.89 | 0.89 |
| 15.0 | 7.5 | 0.91 | 0.88 | 0.92 | 0.94 | 0.94 | 0.95 | 0.94 | 0.94 | 0.94 | 0.94 | 0.94 | 0.92 | 0.91 |
| | | | | | | | | | | | | | | |
| 17.5 | 17.5 | 0.83 | 0.76 | 0.84 | 0.87 | 0.87 | 0.89 | 0.87 | 0.87 | 0.88 | 0.88 | 0.87 | 0.84 | 0.83 |
| 17.5 | 15.0 | 0.86 | 0.78 | 0.84 | 0.89 | 0.90 | 0.88 | 0.88 | 0.89 | 0.89 | 0.89 | 0.89 | 0.85 | 0.85 |
| 17.5 | 10.0 | 0.90 | 0.85 | 0.90 | 0.93 | 0.92 | 0.92 | 0.93 | 0.93 | 0.93 | 0.92 | 0.93 | 0.90 | 0.90 |
| | | | | | | | | | | | | | | |
| 20.0 | 20.0 | 0.83 | 0.76 | 0.83 | 0.87 | 0.87 | 0.87 | 0.87 | 0.87 | 0.87 | 0.87 | 0.87 | 0.83 | 0.83 |
| 20.0 | 17.5 | 0.85 | 0.78 | 0.85 | 0.89 | 0.88 | 0.88 | 0.89 | 0.89 | 0.88 | 0.88 | 0.88 | 0.85 | 0.85 |
| 20.0 | 15.0 | 0.87 | 0.81 | 0.86 | 0.91 | 0.90 | 0.89 | 0.90 | 0.90 | 0.89 | 0.89 | 0.90 | 0.87 | 0.87 |
| 20.0 | 12.5 | 0.89 | 0.83 | 0.89 | 0.92 | 0.91 | 0.91 | 0.92 | 0.92 | 0.91 | 0.92 | 0.92 | 0.89 | 0.89 |
| | | | | | | | | | | | | | | |
| 22.5 | 22.5 | 0.85 | 0.78 | 0.85 | 0.89 | 0.77 | 0.87 | 0.88 | 0.89 | 0.88 | 0.86 | 0.88 | 0.85 | 0.85 |
| 22.5 | 20.0 | 0.86 | 0.79 | 0.85 | 0.89 | 0.88 | 0.88 | 0.89 | 0.88 | 0.87 | 0.88 | 0.89 | 0.85 | 0.86 |
| 22.5 | 15.0 | 0.89 | 0.84 | 0.90 | 0.92 | 0.90 | 0.92 | 0.93 | 0.92 | 0.91 | 0.92 | 0.92 | 0.90 | 0.89 |
| | | | | | | | | | | | | | | |
| 25.0 | 25.0 | 0.85 | 0.79 | 0.86 | 0.88 | 0.87 | 0.88 | 0.89 | 0.88 | 0.87 | 0.88 | 0.89 | 0.86 | 0.86 |
| 25.0 | 22.5 | 0.87 | 0.81 | 0.86 | 0.90 | 0.89 | 0.88 | 0.89 | 0.89 | 0.88 | 0.89 | 0.90 | 0.86 | 0.87 |
| 25.0 | 20.0 | 0.87 | 0.82 | 0.87 | 0.90 | 0.89 | 0.89 | 0.90 | 0.90 | 0.89 | 0.89 | 0.90 | 0.87 | 0.87 |
| 25.0 | 17.5 | 0.89 | 0.83 | 0.88 | 0.9 | 0.91 | 0.89 | 0.91 | 0.91 | 0.90 | 0.90 | 0.91 | 0.88 | 0.89 |

Table 5.5 Relative Efficiencies for OLS vs. IRWLS Analyses When ME is Overspecified ($\beta_1$)

| $\beta_1$ | | -3 | -3 | -3 | -1 | -1 | -1 | -1 | 1 | 1 | 1 | 1 | 3 | 3 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $\beta_{11}$ | | -3 | -1 | 3 | -3 | -1 | 1 | 3 | -3 | -1 | 1 | 3 | -3 | 3 |
| True ME | Spec ME | | | | | | | | | | | | | |
| 2.5 | 2.5 | 0.96 | 0.99 | 0.95 | 0.96 | 0.99 | 0.99 | 0.95 | 0.96 | 0.99 | 0.99 | 0.95 | 0.96 | 0.96 |
| 2.5 | 5.0 | 0.96 | 1.0 | 0.97 | 0.95 | 1.0 | 1.0 | 0.97 | 0.96 | 1.0 | 1.0 | 0.98 | 0.97 | 0.99 |
| 5.0 | 5.0 | 0.90 | 0.99 | 0.90 | 0.89 | 0.98 | 0.98 | 0.89 | 0.89 | 0.99 | 0.98 | 0.88 | 0.90 | 0.89 |
| 5.0 | 7.5 | 0.87 | 0.99 | 0.86 | 0.87 | 0.99 | 0.98 | 0.86 | 0.87 | 0.99 | 0.99 | 0.86 | 0.87 | 0.86 |
| 5.0 | 10.0 | 0.83 | 0.99 | 0.85 | 0.83 | 1.0 | 1.0 | 0.85 | 0.84 | 1.0 | 1.0 | 0.86 | 0.85 | 0.87 |
| 5.0 | 12.5 | 0.83 | 1.03 | 0.85 | 0.83 | 1.0 | 1.0 | 0.85 | 0.84 | 1.0 | 1.1 | 0.86 | 0.85 | 0.87 |
| 7.5 | 7.5 | 0.87 | 0.98 | 0.87 | 0.85 | 0.96 | 0.97 | 0.86 | 0.86 | 0.96 | 0.96 | 0.85 | 0.87 | 0.86 |
| 7.5 | 10 | 0.84 | 0.97 | 0.84 | 0.84 | 0.96 | 0.95 | 0.83 | 0.84 | 0.96 | 0.95 | 0.83 | 0.85 | 0.84 |
| 7.5 | 12.5 | 0.82 | 0.97 | 0.82 | 0.83 | 0.97 | 0.95 | 0.82 | 0.83 | 0.97 | 0.96 | 0.82 | 0.83 | 0.82 |
| 7.5 | 15.0 | 0.82 | 0.97 | 0.81 | 0.82 | 0.98 | 0.96 | 0.81 | 0.82 | 0.98 | 0.96 | 0.81 | 0.82 | 0.81 |
| 12.5 | 12.5 | 0.86 | 0.96 | 0.86 | 0.85 | 0.92 | 0.92 | 0.85 | 0.85 | 0.92 | 0.92 | 0.85 | 0.87 | 0.86 |
| 12.5 | 15.0 | 0.84 | 0.96 | 0.84 | 0.83 | 0.91 | 0.91 | 0.83 | 0.83 | 0.91 | 0.90 | 0.82 | 0.84 | 0.84 |
| 12.5 | 17.5 | 0.83 | 0.95 | 0.83 | 0.82 | 0.90 | 0.90 | 0.82 | 0.82 | 0.91 | 0.90 | 0.82 | 0.84 | 0.82 |
| 12.5 | 20.0 | 0.82 | 0.95 | 0.82 | 0.81 | 0.90 | 0.90 | 0.81 | 0.82 | 0.91 | 0.89 | 0.81 | 0.83 | 0.81 |
| 17.5 | 17.5 | 0.86 | 0.95 | 0.87 | 0.85 | 0.90 | 0.90 | 0.86 | 0.86 | 0.91 | 0.90 | 0.85 | 0.87 | 0.86 |
| 17.5 | 20.0 | 0.85 | 0.95 | 0.86 | 0.84 | 0.88 | 0.89 | 0.84 | 0.84 | 0.90 | 0.89 | 0.84 | 0.86 | 0.85 |
| 17.5 | 22.5 | 0.84 | 0.95 | 0.85 | 0.83 | 0.88 | 0.89 | 0.83 | 0.83 | 0.88 | 0.88 | 0.83 | 0.85 | 0.84 |
| 17.5 | 25.0 | 0.84 | 0.95 | 0.84 | 0.83 | 0.88 | 0.88 | 0.83 | 0.83 | 0.88 | 0.88 | 0.83 | 0.84 | 0.84 |
| 20.0 | 20.0 | 0.87 | 0.95 | 0.88 | 0.86 | 0.89 | 0.91 | 0.87 | 0.86 | 0.90 | 0.90 | 0.87 | 0.88 | 0.88 |
| 20.0 | 25.0 | 0.85 | 0.95 | 0.86 | 0.84 | 0.88 | 0.89 | 0.84 | 0.84 | 0.89 | 0.89 | 0.84 | 0.86 | 0.86 |
| 20.0 | 27.5 | 0.85 | 0.95 | 0.85 | 0.84 | 0.87 | 0.88 | 0.84 | 0.84 | 0.89 | 0.88 | 0.84 | 0.86 | 0.85 |

Table 5.6 Relative Efficiencies for OLS vs. IRWLS Analyses When ME is Overspecified ($\beta_{11}$)

| $\beta_1$ | | -3 | -3 | -3 | -1 | -1 | -1 | -1 | 1 | 1 | 1 | 1 | 3 | 3 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $\beta_{11}$ | | -3 | -1 | 3 | -3 | -1 | 1 | 3 | -3 | -1 | 1 | 3 | -3 | 3 |
| True ME | Spec ME | | | | | | | | | | | | | |
| 2.5 | 2.5 | 0.94 | 0.99 | 0.94 | 0.96 | 0.99 | 0.99 | 0.97 | 0.97 | 0.99 | 0.99 | 0.97 | 0.95 | 0.95 |
| 2.5 | 5.0 | 0.94 | 1.0 | 0.95 | 0.98 | 1.0 | 1.0 | 0.99 | 0.99 | 1.0 | 1.0 | 1.0 | 0.97 | 0.98 |
| 5.0 | 5.0 | 0.87 | 0.93 | 0.88 | 0.91 | 0.99 | 0.98 | 0.91 | 0.90 | 0.98 | 0.99 | 0.91 | 0.87 | 0.87 |
| 5.0 | 7.5 | 0.82 | 0.92 | 0.84 | 0.85 | 0.98 | 0.98 | 0.87 | 0.85 | 0.99 | 0.99 | 0.87 | 0.84 | 0.85 |
| 5.0 | 10.0 | 0.82 | 0.92 | 0.83 | 0.85 | 0.99 | 1.0 | 0.86 | 0.86 | 1.0 | 1.0 | 0.87 | 0.85 | 0.85 |
| 5.0 | 12.5 | 0.81 | 0.96 | 0.83 | 0.84 | 1.0 | 1.0 | 0.87 | 0.86 | 1.0 | 1.0 | 0.87 | 0.85 | 0.85 |
| 7.5 | 7.5 | 0.83 | 0.83 | 0.83 | 0.87 | 0.94 | 0.94 | 0.86 | 0.87 | 0.95 | 0.93 | 0.86 | 0.84 | 0.83 |
| 7.5 | 10.0 | 0.81 | 0.84 | 0.83 | 0.84 | 0.96 | 0.95 | 0.85 | 0.84 | 0.94 | 0.96 | 0.84 | 0.81 | 0.81 |
| 7.5 | 12.5 | 0.78 | 0.81 | 0.80 | 0.79 | 0.94 | 0.94 | 0.81 | 0.80 | 0.95 | 0.96 | 0.81 | 0.80 | 0.80 |
| 7.5 | 15.0 | 0.77 | 0.82 | 0.79 | 0.77 | 0.94 | 0.95 | 0.79 | 0.78 | 0.96 | 0.96 | 0.79 | 0.79 | 0.79 |
| 12.5 | 12.5 | 0.82 | 0.76 | 0.83 | 0.85 | 0.88 | 0.90 | 0.86 | 0.85 | 0.90 | 0.91 | 0.86 | 0.83 | 0.83 |
| 12.5 | 15.0 | 0.81 | 0.73 | 0.80 | 0.84 | 0.88 | 0.88 | 0.83 | 0.85 | 0.90 | 0.87 | 0.83 | 0.81 | 0.80 |
| 12.5 | 17.5 | 0.79 | 0.73 | 0.81 | 0.82 | 0.89 | 0.89 | 0.83 | 0.83 | 0.88 | 0.89 | 0.82 | 0.80 | 0.79 |
| 12.5 | 20.0 | 0.79 | 0.71 | 0.80 | 0.81 | 0.88 | 0.89 | 0.82 | 0.82 | 0.88 | 0.88 | 0.81 | 0.79 | 0.78 |
| 17.5 | 17.5 | 0.83 | 0.76 | 0.84 | 0.87 | 0.87 | 0.89 | 0.87 | 0.87 | 0.88 | 0.88 | 0.87 | 0.84 | 0.83 |
| 17.5 | 20.0 | 0.82 | 0.74 | 0.85 | 0.86 | 0.86 | 0.89 | 0.88 | 0.87 | 0.89 | 0.88 | 0.87 | 0.84 | 0.83 |
| 17.5 | 22.5 | 0.81 | 0.71 | 0.81 | 0.86 | 0.86 | 0.85 | 0.85 | 0.86 | 0.87 | 0.85 | 0.85 | 0.82 | 0.81 |
| 17.5 | 25.0 | 0.81 | 0.70 | 0.80 | 0.85 | 0.86 | 0.85 | 0.84 | 0.85 | 0.87 | 0.84 | 0.84 | 0.81 | 0.80 |
| 20.0 | 20.0 | 0.83 | 0.76 | 0.83 | 0.87 | 0.87 | 0.87 | 0.87 | 0.87 | 0.87 | 0.87 | 0.87 | 0.83 | 0.83 |
| 20.0 | 25.0 | 0.83 | 0.74 | 0.85 | 0.87 | 0.85 | 0.88 | 0.88 | 0.88 | 0.88 | 0.88 | 0.88 | 0.85 | 0.84 |
| 20.0 | 27.5 | 0.82 | 0.73 | 0.85 | 0.86 | 0.85 | 0.88 | 0.88 | 0.87 | 0.88 | 0.87 | 0.87 | 0.84 | 0.83 |

# 6. Design Criteria in the Presence of ME

Popular response surface designs, such as CCDs, have been discussed in earlier chapters. As mentioned previously, these designs are prevalent due to certain characteristics. In many cases, the characteristics are based on the performance of these designs for several *design optimality criteria*. Most of these criteria originate from the ideas of optimal design theory, which is outlined in the work of Kiefer (1959, 1961) and Kiefer and Wolfowitz (1959). Although experimental designs involve several choices about the number of design levels and the number of points at a specified design level, optimality criteria are expressed as single values. The criterion value represents the capabilities of a specific design. The criteria often focus on model estimation or prediction. They usually contain some summary of the coefficient variances or of the prediction variance within a specific range of the design factors. This range of the design factors is called the design space. Because many of these criteria are named by letters such as D, A, and Q, they are often referred to as alphabetic design criteria. Many different design optimality criteria exist for building response surface designs for both linear models (see Myers and Montgomery, 1995) and nonlinear models [Letsinger (1995), Jia (1996), Chiacchierini(1996)], although the more frequently used criteria evaluate designs for linear models.

## 6.1 D-optimality

Perhaps the most commonly adopted design criterion is the D-optimality criterion. D-optimality focuses on the estimation of model coefficients. Recall that in a linear model with homogeneous variance, the covariance matrix of the model coefficients is

$$(X'X)^{-1}\sigma^2,$$

where X is the model matrix for the design and $\sigma^2$ is the variance of $y_i$. When this value is multiplied by $n/\sigma^2$ (to eliminate the nuisance parameter and account for design size), the scaled covariance matrix becomes

$$n(X'X)^{-1} = M^{-1}.$$

This matrix is recognizable as the inverse of the design moment matrix, M, which was discussed briefly in Chapter 1. The D-optimality criterion uses a norm of the $M^{-1}$ matrix to evaluate its properties. The determinant

$$\left|M^{-1}\right| = \frac{1}{|M|},$$

$$\text{where } |M| = \frac{|X'X|}{n^p}$$

is the focus of the D-optimality criterion. Note that p is the number of coefficients in the model, so that X'X is a $p \times p$ matrix. The determinant of the inverse of the moment matrix is also known as the scaled generalized variance of the coefficients (scaled by $n^p/\sigma^2$). The determinant value gives an overall measure of the variability in the coefficient estimates, so that a design which yields a small generalized variance is preferred over a design with a larger generalized variance.

The D-optimality criterion is as follows:

$$D_{opt} = \underset{\mathbf{d} \in \mathbf{D}}{\text{Minimize}} \left|M^{-1}\right| = \underset{\mathbf{d} \in \mathbf{D}}{\text{Maximize}} |M|, \tag{6.1}$$

where $\mathbf{d}$ is the design which satisfies the criteria out of all possible designs $\mathbf{D}$ for a specific design space. It has been shown that minimizing the determinant of $M^{-1}$ is equivalent to minimizing the volume of a $(1-\alpha)100\%$ confidence ellipsoid on the coefficients when the parameter estimates are asymptotically normal (Myers and Montgomery, 1995).

A D-criterion value can be calculated for any design used to estimate a specified model. For the model of interest, the D-optimality criterion allows the comparison of designs of different sizes, since the value of the criterion is a function of n. The D-efficiency of a design $\boldsymbol{d^*}$ can be expressed as

$$D_{eff(d^*)} = \left[ \frac{\frac{1}{n^p{}_{d^*}} \left| \mathbf{X}_{d^*}{}' \mathbf{X}_{d^*} \right|}{\max\limits_{d \in D} \frac{1}{n^p} \left| \mathbf{X}' \mathbf{X} \right|} \right]^{1/p} . \qquad (6.2)$$

An attractive attribute of the D-optimality criterion is availability of the DETMAX algorithm (Mitchell, 1974) for augmenting designs. It has been shown that the point which most greatly increases the D-efficiency of a design is that point in the design space with the highest prediction variance. The prediction variance is given by the expression

$$\mathrm{var}(y(\underline{x}_0)) = \underline{x}_0'(X'X)^{-1}\underline{x}_0,$$

and can be calculated easily for any point in the design space. An experimenter with knowledge of the design space and the model for a given situation can augment an existing design easily. He or she simply calculates the prediction variance at all practical points in the design space (referred to as candidate points) and chooses the point with the greatest prediction variance.

Another attractive feature of the D criterion is the availability of software which can produce D-optimal designs. Procedures such as Proc OPTEX in SAS® (1996) and RS/Discover in RS/1® (1996) are capable of creating D-optimal designs or augmenting existing designs to create the most D-efficient designs based on a list of possible candidate points.

The effects of ME on the D criterion are discussed in the following sections.

## 6.2 D-optimal Designs for Systems Involving ME: First Order Models

Silvey (1980) outlines the theory of optimal designs based on the idea of finite design measures. The theory also outlines properties of optimal designs for certain alphabetic design criteria. It will be demonstrated in this section that the D-optimal design for a first order model with no ME in the design factors is also D-optimal when there is ME present in a single design factor.

In order to define the property required for a D-optimal design, a few definitions are required. The expression $L(\underline{\beta}, X)$ represents the likelihood function of the data. The information matrix for the data is expressed as

$$\mathbf{I}(X, \underline{\beta}) = -E\left(\frac{\partial^2 \ln L}{\partial\underline{\beta}'\partial\underline{\beta}}\right).$$

The term $\mathbf{J}(\underline{x}, \underline{\beta})$ will represent the information matrix for a single point in the design space. It may be simpler to think of $\mathbf{J}(\underline{x}, \underline{\beta})$ as the information at a candidate point in the design space. Using these expressions, the requirement for a design to be D-optimal can be defined.

Consider an n-point design for a model with p coefficients. In the case of D-optimality, a design $\boldsymbol{d^*}$ is optimal for fixed $\underline{\beta}$ if and only if

$$n\cdot\text{Trace}(\mathbf{J}(\underline{x}, \underline{\beta})\cdot\mathbf{I}(\boldsymbol{d^*}, \underline{\beta})^{-1}) \le p \quad \forall \ \underline{x} \in \mathcal{X}, \tag{6.3}$$

where $\mathbf{I}(\boldsymbol{d^*}, \underline{\beta})$ is the information matrix for the design $\boldsymbol{d^*}$, $\mathbf{J}(\underline{x}, \underline{\beta})$ is as previously defined, and $\mathcal{X}$ is the set of all possible design points in the design space. Because the model of interest is first order, p = k + 1. For a linear model with no ME in the design factors, the optimal design for a first order model has been shown to be the orthogonal design with each factor containing n/2 points at the greatest value in the design region and n/2 points at the least value in the design region (Myers and Montgomery, 1995). When these values are conveniently coded to 1 and -1, respectively, the information matrix for the design becomes

$$\mathbf{I}(\boldsymbol{d^*}, \underline{\beta}) = n\cdot\mathbf{I}_p,$$

$$\text{and } \mathbf{J}(\underline{x}, \underline{\beta}) = \begin{bmatrix} 1 & x_{1i} & x_{2i} & x_{3i} & \cdots & x_{ki} \\ x_{1i} & x^2_{1i} & x_{1i}x_{2i} & x_{1i}x_{3i} & \cdots & x_{1i}x_{ki} \\ x_{2i} & x_{1i}x_{2i} & x^2_{2i} & x_{2i}x_{3i} & \cdots & x_{2i}x_{ki} \\ x_{3i} & x_{1i}x_{3i} & x_{2i}x_{3i} & x^2_{3i} & \cdots & x_{3i}x_{ki} \\ \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\ x_{ki} & x_{1i}x_{ki} & x_{2i}x_{ki} & x_{3i}x_{ki} & \cdots & x^2_{ki} \end{bmatrix}. \tag{6.4}$$

The expression in equation 6.3 becomes

$$n\cdot\text{Trace}(\mathbf{J}(\underline{x}, \underline{\beta})\cdot\mathbf{I}(\boldsymbol{d^*}, \underline{\beta})^{-1}) = n\cdot\text{Trace}(\mathbf{J}(\underline{x}, \underline{\beta})\cdot n^{-1}\mathbf{I}_p)$$

$$= \text{Trace}(\mathbf{J}(\underline{x}, \underline{\beta})) \quad = \quad 1 + \sum_{j=1}^{k} x^2_{ji} \ \le p \qquad \forall \ \underline{x} \in \mathcal{X},$$

with equality only at the design points which place all factors at the greatest or least value in the design space, so that $\mathbf{J}(\underline{x}, \underline{\beta}) = \mathbf{I}_p$.

Recall that for the first order model involving ME in the design levels, the variance of individual observations is inflated due to the ME. This inflation is homogeneous across the design region. Optimal design theory can be applied to the first order model in certain situations. A first order model with normal random errors and normally distributed Berkson error will be considered here. The first order model with k variables and ME in variable $x_1$ is

$$y_i = \beta_0 + \sum_{j=1}^{k} \beta_j X_{ji} + \beta_1 u_i + \varepsilon_i, \ \ i = 1,\ldots, n.$$

$$\varepsilon_i \sim N(0,\sigma_0^2) \ \text{ and } u_i \sim N(0,\sigma_1^2).$$

The likelihood for the Berkson error model can be expressed as follows (Carroll, Ruppert, and Stefanski, 1995):

$$L = \int f(y|x,\beta,\sigma_0^2)\cdot f(x|X,\sigma_1^2)\partial x. \qquad (6.5)$$

Denoting $\dfrac{1}{\sqrt{2\Pi\sigma_0^2}}$ as $k_0$ and $\dfrac{1}{\sqrt{2\Pi\sigma_1^2}}$ as $k_1$, the specified densities can be substituted and the expression simplified.

$$L = \int f(y|x,\beta,\sigma_0^2)\cdot f(u|\sigma_1^2)\partial u$$

$$= \int k_0 \cdot e^{-\frac{(y-X\beta-\beta_1 u)^2}{2\sigma_0^2}} \cdot k_1 \cdot e^{-\frac{u^2}{2\sigma_1^2}}\partial u$$

$$= \left(k_0 \cdot e^{-\frac{(y-X\beta)^2}{2\sigma_0^2}}\right) \int k_1 \cdot e^{-\frac{((\sigma_1^2\beta_1^2+\sigma_0^2)u^2-((2\beta_1\sigma_1^2[y-X\beta])u}{2\sigma_1^2\sigma_0^2}} \partial u$$

$$= \left(k_0 \cdot e^{-\frac{(y-X\beta)^2}{2\sigma_0^2}}\right) \int k_1 \cdot \frac{\sqrt{\frac{\sigma_0^2}{\sigma_1^2\beta_1^2+\sigma_0^2}}}{\sqrt{\frac{\sigma_0^2}{\sigma_1^2\beta_1^2+\sigma_0^2}}} \cdot e^{-\frac{\left(u-\frac{\beta_1\sigma_1^2[y-X\beta]}{\sigma_1^2\beta_1^2+\sigma_0^2}\right)^2-\left(\frac{\beta_1\sigma_1^2[y-X\beta]}{\sigma_1^2\beta_1^2+\sigma_0^2}\right)^2}{2\frac{\sigma_1^2\sigma_0^2}{\sigma_1^2\beta_1^2+\sigma_0^2}}} \partial u$$

$$= k_0 \cdot e^{-\frac{(y-X\beta)^2}{2\sigma_0^2}} \cdot e^{\frac{\left[\frac{(\beta_1\sigma_1^2[y-X\beta])^2}{\sigma_1^2\beta_1^2+\sigma_0^2}\right]}{2\sigma_0^2\sigma_1^2}} \cdot \sqrt{\frac{\sigma_0^2}{\sigma_1^2\beta_1^2+\sigma_0^2}}$$

$$= \frac{1}{\sqrt{2\Pi(\sigma_1^2\beta_1^2+\sigma_0^2)}} \cdot e^{-\frac{(y-X\beta)^2}{2(\sigma_1^2\beta_1^2+\sigma_0^2)}}. \qquad (6.6)$$

From equation (6.6), it can be seen that

$$y_i \sim N(\underline{X}_i'\underline{\beta},\ \sigma_1^2\beta_1^2 + \sigma_0^2)$$

when $\varepsilon$ and $u$ are both normally distributed and the mean of $y$ can be expressed as a first order model in X. The Fisher Information matrix for this model is expressed as

$$\mathbf{I}(X, \beta) = A^{-1}\begin{bmatrix} \sum_{i=1}^{n} 1 & \sum_{i=1}^{n} X_{1i} & \sum_{i=1}^{n} X_{2i} & \sum_{i=1}^{n} X_{3i} & \cdots & \sum_{i=1}^{n} X_{ki} \\ \sum_{i=1} X_{1i} & \sum_{i=1} X_{1i}^2 + \mathbf{C} & \sum_{i=1}^{n} X_{1i}X_{2i} & \sum_{i=1}^{n} X_{1i}X_{3i} & \cdots & \sum_{i=1}^{n} X_{1i}X_{ki} \\ \sum_{i=1} X_{2i} & \sum_{i=1}^{n} X_{1i}X_{2i} & \sum_{i=1}^{n} X_{2i}^2 & \sum_{i=1} X_{2i}X_{3i} & \cdots & \sum_{i=1}^{n} X_{2i}X_{ki} \\ \sum_{i=1} X_{3i} & \sum_{i=1} X_{1i}X_{3i} & \sum_{i=1}^{n} X_{2i}X_{3i} & \sum_{i=1}^{n} X_{3i}^2 & \cdots & \sum_{i=1} X_{3i}X_{ki} \\ \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\ \sum_{i=1} X_{ki} & \sum_{i=1}^{n} X_{1i}X_{ki} & \sum_{i=1}^{n} X_{2i}X_{ki} & \sum_{i=1} X_{3i}X_{ki} & \cdots & \sum_{i=1}^{n} X_{ki}^2 \end{bmatrix}, \qquad (6.7)$$

where $A = \sigma_1^2\beta_1^2 + \sigma_0^2$, and $\mathbf{C} = \sigma_1^2 + \dfrac{\beta_1^2\sigma_1^4\sigma_0^2 - 2\beta_1^4\sigma_1^6 - \sigma_1^2\sigma_0^4}{\beta_1^2\sigma_1^2 + \sigma_0^2}$.

To show that the D-optimal design in the case of no ME is still optimal in this case, consider the value of $\mathbf{I}(\boldsymbol{d}^*, \underline{\beta})^{-1}$ and $\mathbf{J}(\underline{x}, \underline{\beta})$ for the case in which ME is present:

$$\mathbf{I}(\boldsymbol{d}^*, \underline{\beta})^{-1} = n^{-1}\begin{bmatrix} 1 & 0 & 0 & 0 & \dots & 0 \\ 0 & (1+\mathbf{C})^{-1} & 0 & 0 & \dots & 0 \\ 0 & 0 & 1 & 0 & \dots & 0 \\ 0 & 0 & 0 & 1 & \dots & 0 \\ \dots & \dots & \dots & \dots & \dots & \dots \\ 0 & 0 & 0 & 0 & \dots & 1 \end{bmatrix}. \tag{6.8}$$

$$\mathbf{J}(\underline{x}, \underline{\beta}) = \begin{bmatrix} 1 & 0 & 0 & 0 & \dots & 0 \\ 0 & X^2_{1i}+\mathbf{C} & 0 & 0 & \dots & 0 \\ 0 & 0 & X^2_{2i} & 0 & \dots & 0 \\ 0 & 0 & 0 & X^2_{3i} & \dots & 0 \\ \dots & \dots & \dots & \dots & \dots & \dots \\ 0 & 0 & 0 & 0 & \dots & X^2_{ki} \end{bmatrix}, \tag{6.9}$$

so that

$$n\cdot\mathrm{Trace}(\mathbf{J}(\underline{x}, \underline{\beta})\cdot\mathbf{I}(\boldsymbol{d}^*, \underline{\beta})^{-1}) = 1 + (X^2_{1i} + \mathbf{C})\cdot(1+\mathbf{C})^{-1} + \sum_{j=2}^{k} X^2_{ji}$$

$$\leq p = k + 1,$$

with equality only at the design points which place all factors at ±1. Thus the D-optimal design remains the same regardless of ME in the first design factor.

## 6.3 Designs for Systems Involving ME: Second Order Models

In the case of a second order model, the likelihood for even the simplest single design factor experiment involving ME in the design levels is much more complex. The maximum likelihood expressions involve mixtures of normal and chi-squared distributions. The development of design optimality from a classical perspective is unfortunately impractical. However, the ideas behind the previously developed design criterion can lead to interesting design solutions when certain information is available about the model.

Consider a single factor situation involving ME in the design levels. Recall the covariance matrix of $\underline{\beta}$, the vector of model coefficients, is

$$\mathrm{Var}(\underline{\beta}) = (X^{*\prime}V^{-1}X^*)^{-1}.$$

It is obvious that information about the model coefficients themselves is required to completely specify the covariance matrix in this situation, since V is a function of at least a subset of $\underline{\beta}$. Work summarized in Chapters 4 and 5 indicates that balanced designs are often robust to the effect of incorrect analysis in a ME situation. In other words, the difference between the correct (IRWLS) and naïve (OLS) analyses of the data is negligible unless the standard deviation of the ME is a significant percentage of the range of *X*.

Based on these results, a two stage procedure was developed to make use of the information about the model coefficients from a "good" first stage design. The criterion for the procedure is outlined in the following section. The development of the criterion will be restricted to situations in which only one of the design variables involves ME.

## 6.4 The $D_{ME}$ Augmentation Criterion

This section presents a design criterion similar to the D criterion, because it is based on the generalized variance of the model coefficients. It is assumed that ME is present in the design levels of $X_1$. Since the generalized variance is a function of the model coefficients as previously mentioned, information about $\underline{\beta}$ is required. The criterion presented here is specifically designed to compare augmented designs in a two-stage procedure. The $D_{ME}$ criterion minimizes the determinant of the covariance matrix of the model coefficients for a complete two-stage design. However, the minimization is conditional on the design implemented in the intial stage of the experiment. The criterion is expressed as follows:

$$D_{ME} = \underset{\boldsymbol{d}_2 | \boldsymbol{d}_1 \in \mathbf{D}}{\text{Minimize}} \quad n^p \ \mathrm{DET}\left(X^{*\prime}\hat{V}^{-1}X^{*}\right)^{-1} \tag{6.10}$$

$$= \underset{\boldsymbol{d}_2 | \boldsymbol{d}_1 \in \mathbf{D}}{\text{Maximize}} \quad \frac{1}{n^p} \mathrm{DET}\left(X^{*\prime}\hat{V}^{-1}X^{*}\right),$$

where $\mathbf{D}$ is the set of all possible designs for the given situation, $\boldsymbol{d}_1$ is the initial design chosen by the experimenter, and $\boldsymbol{d}_2$ is one possible second-stage design. Note that n is the number of design points in the entire design, so that $n_{\boldsymbol{d}_1} + n_{\boldsymbol{d}_2} = n$. This design criterion requires knowledge of the ME variance, but only through the estimate of V. The modified model matrix, $X^*$, may be replaced by the usual model matrix X. The following theorem proves this result.

Theorem 2: *Consider a k-factor experimental design for a second order model with ME in a single design factor. The determinant of the covariance matrix of the coefficients depends on the ME variance only through the variance of $y_i$.*

Proof: Recall the form of the model matrix $X^*$. In a two-factor situation where ME is present in the first design variable, the model matrix is as follows:

$$X^* = \begin{bmatrix} 1 & X_{11} & X_{21} & X_{11}\cdot X_{21} & X_{11}^2+\sigma_1^2 & X_{21}^2 \\ 1 & X_{12} & X_{22} & X_{12}\cdot X_{22} & X_{12}^2+\sigma_1^2 & X_{22}^2 \\ & & & \cdots & & \\ 1 & X_{1n} & X_{2n} & X_{1n}\cdot X_{2n} & X_{1n}^2+\sigma_1^2 & X_{2n}^2 \end{bmatrix}.$$

Notice that only the column involving the quadratic term in $X_1$ differs from the model matrix in a non-ME situation, X. This is true regardless of the number of factors in the design if only $X_1$ involves ME. Then the model matrix $X^*$ can be rewritten as

$$X^* = X + \left[\underline{0} \quad \underline{0} \quad \underline{0} \quad \underline{0} \quad \sigma_1^2\cdot X[,1] \quad \underline{0}\right],$$

where X[,1] is the first column of X.

Now consider the form of the matrix $(X^{*\prime}\hat{V}^{-1}X^*)$:

$$\begin{bmatrix}
\sum_{i=1}^{n}\frac{1}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}}{v_i} & \sum_{i=1}^{n}\frac{X_{2i}}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}X_{2i}}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}^2+\sigma_1^2}{v_i} & \sum_{i=1}^{n}\frac{X_{2i}^2}{v_i} \\
\sum_{i=1}^{n}\frac{X_{1i}}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}^2}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}X_{2i}}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}^2X_{2i}}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}^3+X_{1i}\sigma_1^2}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}X_{2i}^2}{v_i} \\
\sum_{i=1}^{n}\frac{X_{2i}}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}\cdot X_{2i}}{v_i} & \sum_{i=1}^{n}\frac{X_{2i}^2}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}X_{2i}^2}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}^2X_{2i}+X_{2i}\sigma_1^2}{v_i} & \sum_{i=1}^{n}\frac{X_{2i}^3}{v_i} \\
\sum_{i=1}^{n}\frac{X_{1i}\cdot X_{2i}}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}^2\cdot X_{2i}}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}X_{2i}^2}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}^2X_{2i}^2}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}^3X_{2i}+X_{1i}X_{2i}\sigma_1^2}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}X_{2i}^3}{v_i} \\
\sum_{i=1}^{n}\frac{X_{1i}^2+\sigma_1^2}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}^3+X_{1i}\sigma_1^2}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}^2X_{2i}+X_{2i}\sigma_1^2}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}^3X_{2i}+X_{1i}X_{2i}\sigma_1^2}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}^4+\sigma_1^2(2X_{1i}^2+\sigma_1^2)}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}^2X_{2i}^2+X_{2i}^2\sigma_1^2}{v_i} \\
\sum_{i=1}^{n}\frac{X_{2i}^2}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}\cdot X_{2i}^2}{v_i} & \sum_{i=1}^{n}\frac{X_{2i}^3}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}X_{2i}^3}{v_i} & \sum_{i=1}^{n}\frac{X_{1i}^2X_{2i}^2+X_{2i}^2\sigma_1^2}{v_i} & \sum_{i=1}^{n}\frac{X_{2i}^4}{v_i}
\end{bmatrix}$$

$$= (X'\hat{V}^{-1}X)^* + \sigma_1^2\cdot(X'\hat{V}^{-1}X)^*[5,],$$

$$= \{(X'\hat{V}^{-1}X) + \sigma_1^2\cdot(X'\hat{V}^{-1}X)[,5]\} + \sigma_1^2\cdot(X'\hat{V}^{-1}X)^*[5,], \qquad (6.11)$$

where $(X'\hat{V}^{-1}X)[,5]$ is the fifth column of $(X'\hat{V}^{-1}X)$, and $(X'\hat{V}^{-1}X)^*[5,]$ is the fifth row of the matrix $(X'\hat{V}^{-1}X) + \sigma_1^2\cdot(X'\hat{V}^{-1}X)[,5]$.

It is true for any n *x* n matrix that if a scalar multiple of any row (or column) of the matrix is added to any other row (or column) of the matrix, the determinant of the matrix remains unchanged (Basilevsky, 1983). Then

$$|X'\hat{V}^{-1}X| = |(X'\hat{V}^{-1}X)^*|$$

$$= |X^{*\prime}\hat{V}^{-1}X^*| = \frac{1}{\left|\left(X^{*\prime}\hat{V}^{-1}X^*\right)^{-1}\right|}.$$

Thus the determinant of the covariance matrix of the coefficients depends on the ME variance only through the variance of $y_i$.

The theorem indicates that the $D_{ME}$ design criterion only requires knowledge of the ME variance through the V matrix, which is encouraging from a design standpoint. Results from Chapter 5 suggest that overestimation of the ME variance is more desirable than underestimation, so a researcher may want to use this guideline when deciding on the specification of ME for the design augmentation as well.

### 6.4.1 Criterion Methodology

Suppose a researcher wants to augment an existing design, but he or she feels that there is ME associated with a particular design variable. A list of candidate points for the design space is required in order to choose the best point for augmentation. Using the variance information from the initial design, an optimal point is identified and the experiment takes place at the chosen settings. The model coefficients are re-estimated and the next point is chosen based on the current coefficient estimates. This design augmentation procedure requires an experimental situation in which the experimental runs are not performed simultaneously. For this reason, the $D_{ME}$ criterion may not be suitable for all experimental designs, but it can be advantageous in some situations.

### 6.4.2 Design Efficiency for the $D_{ME}$ criterion: Single Factor Designs

The performance of designs chosen by the $D_{ME}$ criterion was evaluated for a single factor, second order model (see equation 4.4). The augmented designs chosen by the criterion were compared to the "best" augmented design ignoring ME in the design levels. For this reason, each design chosen by the $D_{ME}$ criterion was compared to a corresponding D-optimal design which ignored the presence of ME.

Initially, an $n_{\boldsymbol{d}_1}$-point design was chosen for the first stage of the experiment. Then a D-optimal design was created using the DETMAX algorithm (Mitchell, 1974) to augment the design of choice by $n_{\boldsymbol{d}_2}$ points. Next a $D_{ME}$-optimal design was created using the methodology outlined in the Section 6.4.1. Both designs were analyzed using IRWLS and accounting for the ME present in the design levels. By including the ME in the analysis of each design, the difference in the performance of the two designs is strictly based on the criterion used to choose the second stage of the design.

The comparison of D-optimal and $D_{ME}$-optimal designs was based on the ratio of the determinants of the covariance matrices for the designs,

$$D/D_{ME}\text{ efficiency} = \left[\frac{\left|(X^{*\prime}V^{-1}X^{*})^{-1}_{D_{ME}}\right|}{\left|(X^{*\prime}V^{-1}X)^{-1}_{D}\right|}\right]^{1/3}. \qquad (6.12)$$

This ratio expresses the efficiency of the D-optimal design in relation to the $D_{ME}$-optimal design. Note that the 1/3rd power of the ratio of the determinants is required, because there are three coefficients estimated for the model ($\beta_0$, $\beta_1$, $\beta_{11}$).

However, the second stage design based on the $D_{ME}$ criterion is a random variable, since it is a function of the variance information obtained in the first stage. In order to evaluate the design, the variance of the coefficients ($\underline{b}$) must be evaluated in the presence of the random variable, $\boldsymbol{d}_2$. If X2 is the partition of the model matrix pertaining to the second stage design $\boldsymbol{d}_2$, the variance of $\underline{b}$ can be expressed as follows:

$$\mathrm{Var}(\underline{b}) = E_{X2}[\ \mathrm{Var}(\ \underline{b}\ |\ X2\ )\ ] + \mathrm{Var}_{X2}[\ E(\ \underline{b}\ |\ X2\ )\ ]. \qquad (6.13)$$

Because the coefficient estimates are the result of Generalized Least Squares, they are unbiased regardless of the model matrix $X^*$. This means the second term in the right-hand side of equation (6.13) reduces to $Var_{X2}[\ \underline{\beta}\ ] = 0$, so that

$$Var(\underline{b}) = E_{X2}[\ Var(\ \underline{b} \mid X2\ )\ ].$$

The resulting expression indicates that the covariance matrix must be averaged across the designs created during simulation in order to accurately arrive at the covariance matrix for $\underline{b}$. Thus the covariance matrices are calculated for each simulated data set, and then the determinant of the average covariance matrix is calculated for the $D_{ME}$ design criterion. Note that the covariance matrix remains unchanged for the D-optimal design, so no simulation is necessary to calculate the determinant.

Several different design situations were considered for the comparison of the $D_{ME}$ criterion to the D criterion. For each design, the initial design, candidate points, and D-optimal second stage design are presented in Table 6.1. In the first comparison, the five-point balanced design considered in Chapter 4 was used as the first stage design. The design was augmented to ten points by both methods. A second comparison augmented the ten-point balanced design to twenty points. The third design situation involved augmenting the five-point balanced design to fifteen points. A fourth comparison augmented a fifteen-point design with seven center runs to thirty points. Each of the designs were augmented from a list of candidate points which included values between and including -2 and 2 in increments of 0.10. Finally, the last comparison augmented an unbalanced ten-point design to twenty points. The candidate points for this design were all values between and including -1 to 3 by 0.10.

Results for the design criterion comparisons are summarized in Table 6.2 - Table 6.4. The design efficiencies appear in Table 6.2, and the efficiencies of individual coefficient estimation are presented in Table 6.3 ($\beta_1$) and Table 6.4 ($\beta_{11}$). The results of these comparisons show little difference in the estimation performance of the $D_{ME}$ and the D criteria. However, in the case of the unbalanced design (Design 5), the efficiencies and the individual coefficient variances are slightly better for the designs based on the $D_{ME}$ criterion. Performance evaluation for the $D_{ME}$ criterion with a two factor design is presented in Chapter 8.

Table 6.1 Designs for D and $D_{ME}$ Criterion Comparison

| | |
|---|---|
| **Design 1** | |
| Initial Design | -2, -1, 0, 1, 2 |
| Candidate Points | -2 to 2 by 0.10 |
| D-optimal 2nd Stage Design | -2, -2, 0, 2, 2 |
| **Design 2** | |
| Initial Design | -2, -2, -1, -1, 0, 0, 1, 1, 2, 2 |
| Candidate Points | -2 to 2 by 0.10 |
| D-optimal 2nd Stage Design | -2, -2, -2, -2, 0, 0, 2, 2, 2 |
| **Design 3** | |
| Initial Design | -2, -1, 0, 1, 2 |
| Candidate Points | -2 to 2 by 0.10 |
| D-optimal 2nd Stage Design | -2, -2, -2, 0, 0, 0, 2, 2, 2, 2 |
| **Design 4** | |
| Initial Design | -2, -2, -1, -1, 0, 0, 0, 0, 0, 0, 0, 1, 1, 2, 2 |
| Candidate Points | -2 to 2 by 0.10 |
| D-optimal 2nd Stage Design | -2, -2, -2, -2, -2, -2, -2, 0, 2, 2, 2, 2, 2, 2, 2 |
| **Design 5** | |
| Initial Design | -1, -1, 0, 0, 1, 1, 2, 2, 3, 3 |
| Candidate Points | -1 to 3 by 0.10 |
| D-optimal 2nd Stage Design | -1, -1, -1, -1, 1, 1, 3, 3, 3, 3 |

Table 6.2 Design Efficiencies for D-optimal vs. $D_{ME}$ Designs

| Design 1 | | | | | | |
|---|---|---|---|---|---|---|
| $(\beta_1, \beta_{11})$ | (-1, 1) | (-1, 2) | (-1, 3) | ( 1, 1) | ( 1, 2) | ( 1, 3) |
| ME (% of Range) | | | | | | |
| 5% | 1.0006 | 1.0011 | 1.0018 | 1.0005 | 1.0005 | 1.0016 |
| 10% | 0.9974 | 0.9973 | 1.0017 | 0.9974 | 0.9973 | 1.0017 |
| 15% | 0.9916 | 0.9981 | 1.0066 | 0.9913 | 0.9984 | 1.0068 |
| 20% | 0.9910 | 1.0039 | 1.0112 | 0.9909 | 1.0032 | 1.0103 |
| Design 2 | | | | | | |
| $(\beta_1, \beta_{11})$ | (-1, 1) | (-1, 2) | (-1, 3) | ( 1, 1) | ( 1, 2) | ( 1, 3) |
| ME (% of Range) | | | | | | |
| 5% | 0.9993 | 0.9986 | 0.9964 | 0.9993 | 0.9988 | 0.9964 |
| 10% | 0.9943 | 0.9880 | 0.9868 | 0.9943 | 0.9880 | 0.9869 |
| 15% | 0.9859 | 0.9853 | 0.9902 | 0.9859 | 0.9854 | 0.9904 |
| 20% | 0.9836 | 0.9911 | 0.9967 | 0.9828 | 0.9904 | 0.9964 |
| Design 3 | | | | | | |
| $(\beta_1, \beta_{11})$ | (-1, 1) | (-1, 2) | (-1, 3) | ( 1, 1) | ( 1, 2) | ( 1, 3) |
| ME (% of Range) | | | | | | |
| 5% | 0.9987 | 0.9969 | 0.9967 | 0.9984 | 0.9965 | 0.9966 |
| 10% | 0.9894 | 0.9884 | 0.9938 | 0.9883 | 0.9885 | 0.9944 |
| 15% | 0.9792 | 0.9893 | 1.0015 | 0.9783 | 0.9893 | 1.0013 |
| 20% | 0.9776 | 0.9967 | 1.0075 | 0.9766 | 0.9969 | 1.0077 |
| Design 4 | | | | | | |
| $(\beta_1, \beta_{11})$ | (-1, 1) | (-1, 2) | (-1, 3) | ( 1, 1) | ( 1, 2) | ( 1, 3) |
| ME (% of Range) | | | | | | |
| 5% | 1.0000 | 0.9989 | 0.9991 | 1.0000 | 0.9989 | 0.9991 |
| 10% | 0.9975 | 0.9967 | 0.9970 | 0.9975 | 0.9967 | 0.9970 |
| 15% | 0.9947 | 0.9957 | 0.9975 | 0.9948 | 0.9957 | 0.9975 |
| 20% | 0.9935 | 0.9968 | 0.9987 | 0.9936 | 0.9968 | 0.9988 |
| Design 5 | | | | | | |
| $(\beta_1, \beta_{11})$ | (-1, 1) | (-1, 2) | (-1, 3) | ( 1, 1) | ( 1, 2) | ( 1, 3) |
| ME (% of Range) | | | | | | |
| 5% | 0.9993 | 0.9874 | 0.9677 | 0.9948 | 0.9798 | 0.9663 |
| 10% | 0.9943 | 0.9581 | 0.9440 | 0.9801 | 0.9634 | 0.9605 |
| 15% | 0.9859 | 0.9521 | 0.9474 | 0.9733 | 0.9643 | 0.9631 |
| 20% | 0.9828 | 0.9598 | 0.9573 | 0.9731 | 0.9671 | 0.9655 |

Table 6.3 Ratio of IRWLS Var ($\beta_1$) to OLS Var ($\beta_1$)

| Design 1 | | | | | | |
|---|---|---|---|---|---|---|
| ($\beta_1$, $\beta_{11}$) | (-1, 1) | (-1, 2) | (-1, 3) | ( 1, 1) | ( 1, 2) | ( 1, 3) |
| ME (% of Range) | | | | | | |
| 5% | 1.0916 | 1.0746 | 1.0717 | 1.0819 | 1.0560 | 1.0487 |
| 10% | 1.0083 | 1.0139 | 1.0347 | 1.0226 | 1.0418 | 1.0710 |
| 15% | 1.0611 | 1.0295 | 1.0302 | 1.0682 | 1.0529 | 1.0456 |
| 20% | 0.9812 | 0.9881 | 0.9897 | 0.9575 | 0.9895 | 1.0135 |
| Design 2 | | | | | | |
| ($\beta_1$, $\beta_{11}$) | (-1, 1) | (-1, 2) | (-1, 3) | ( 1, 1) | ( 1, 2) | ( 1, 3) |
| ME (% of Range) | | | | | | |
| 5% | 1.0011 | 1.0073 | 1.0193 | 0.9803 | 1.0429 | 1.0569 |
| 10% | 1.0208 | 1.0101 | 1.0302 | 1.0362 | 1.0464 | 1.0409 |
| 15% | 1.0281 | 1.0524 | 1.0564 | 0.9669 | 0.9563 | 0.9619 |
| 20% | 1.0415 | 1.0927 | 1.0923 | 1.0623 | 1.0633 | 1.0906 |
| Design 3 | | | | | | |
| ($\beta_1$, $\beta_{11}$) | (-1, 1) | (-1, 2) | (-1, 3) | ( 1, 1) | ( 1, 2) | ( 1, 3) |
| ME (% of Range) | | | | | | |
| 5% | 0.9799 | 0.9740 | 0.9725 | 0.9958 | 0.9985 | 1.0151 |
| 10% | 0.9717 | 1.0043 | 1.0246 | 1.1242 | 1.0452 | 1.0417 |
| 15% | 0.9231 | 0.9242 | 0.9533 | 1.0547 | 1.0094 | 1.0106 |
| 20% | 0.9708 | 0.9730 | 0.9780 | 1.0686 | 1.0239 | 1.0040 |
| Design 4 | | | | | | |
| ($\beta_1$, $\beta_{11}$) | (-1, 1) | (-1, 2) | (-1, 3) | ( 1, 1) | ( 1, 2) | ( 1, 3) |
| ME (% of Range) | | | | | | |
| 5% | 1.0044 | 1.0240 | 1.0222 | 0.9380 | 0.9654 | 0.9707 |
| 10% | 0.9498 | 0.9368 | 0.9260 | 1.0013 | 0.9693 | 0.9574 |
| 15% | 0.9813 | 0.9479 | 0.9399 | 0.9621 | 0.9380 | 0.9278 |
| 20% | 0.9942 | 1.0235 | 1.0393 | 0.9891 | 1.0184 | 1.0224 |
| Design 5 | | | | | | |
| ($\beta_1$, $\beta_{11}$) | (-1, 1) | (-1, 2) | (-1, 3) | ( 1, 1) | ( 1, 2) | ( 1, 3) |
| ME (% of Range) | | | | | | |
| 5% | 1.0292 | 1.0093 | 0.9843 | 1.0551 | 1.0179 | 0.9668 |
| 10% | 0.9469 | 0.9529 | 0.9391 | 0.9511 | 0.9187 | 0.9070 |
| 15% | 0.9506 | 0.9045 | 0.8874 | 0.8735 | 0.8560 | 0.8625 |
| 20% | 0.9374 | 0.9201 | 0.9022 | 0.9171 | 0.8867 | 0.8927 |

Table 6.4 Ratio of IRWLS Var ($\beta_{11}$) to OLS Var ($\beta_{11}$)

| Design 1 | | | | | | |
|---|---|---|---|---|---|---|
| ($\beta_1$, $\beta_{11}$) | (-1, 1) | (-1, 2) | (-1, 3) | ( 1, 1) | ( 1, 2) | ( 1, 3) |
| ME (% of Range) | | | | | | |
| 5% | 0.9592 | 1.0039 | 1.0143 | 0.9345 | 0.9214 | 0.9376 |
| 10% | 0.9820 | 1.0558 | 1.0317 | 1.0231 | 1.0177 | 1.0276 |
| 15% | 1.0012 | 1.0357 | 1.0360 | 0.9567 | 1.0431 | 1.0273 |
| 20% | 0.9961 | 1.0106 | 1.0456 | 0.9789 | 1.0130 | 1.0254 |
| Design 2 | | | | | | |
| ($\beta_1$, $\beta_{11}$) | (-1, 1) | (-1, 2) | (-1, 3) | ( 1, 1) | ( 1, 2) | ( 1, 3) |
| ME (% of Range) | | | | | | |
| 5% | 1.0310 | 1.0372 | 1.0420 | 1.0131 | 0.9864 | 0.9609 |
| 10% | 0.9455 | 1.0158 | 1.0280 | 0.9511 | 1.0033 | 1.0182 |
| 15% | 0.8570 | 0.9023 | 0.9144 | 0.8754 | 0.9373 | 0.9317 |
| 20% | 0.9337 | 0.9631 | 0.9896 | 0.9374 | 0.9818 | 0.9945 |
| Design 3 | | | | | | |
| ($\beta_1$, $\beta_{11}$) | (-1, 1) | (-1, 2) | (-1, 3) | ( 1, 1) | ( 1, 2) | ( 1, 3) |
| ME (% of Range) | | | | | | |
| 5% | 1.0430 | 1.0541 | 1.0603 | 0.9850 | 0.9760 | 0.9665 |
| 10% | 1.0004 | 1.0186 | 1.0516 | 1.0210 | 1.0000 | 0.9888 |
| 15% | 0.9628 | 0.9766 | 0.9955 | 0.9995 | 0.9967 | 1.0275 |
| 20% | 0.8718 | 0.9152 | 0.9633 | 0.9138 | 0.9163 | 0.9345 |
| Design 4 | | | | | | |
| ($\beta_1$, $\beta_{11}$) | (-1, 1) | (-1, 2) | (-1, 3) | ( 1, 1) | ( 1, 2) | ( 1, 3) |
| ME (% of Range) | | | | | | |
| 5% | 1.0568 | 1.0487 | 1.0644 | 1.0220 | 1.0066 | 1.0046 |
| 10% | 0.9904 | 0.9985 | 0.9987 | 1.0564 | 1.0475 | 1.0334 |
| 15% | 1.0270 | 1.0120 | 0.9942 | 1.0409 | 1.0238 | 0.9900 |
| 20% | 0.9624 | 0.9942 | 0.9877 | 0.9738 | 0.9864 | 0.9748 |
| Design 5 | | | | | | |
| ($\beta_1$, $\beta_{11}$) | (-1, 1) | (-1, 2) | (-1, 3) | ( 1, 1) | ( 1, 2) | ( 1, 3) |
| ME (% of Range) | | | | | | |
| 5% | 1.0131 | 0.9586 | 0.9338 | 1.0172 | 0.9489 | 0.9309 |
| 10% | 0.9511 | 0.9413 | 0.9165 | 0.9022 | 0.8929 | 0.8862 |
| 15% | 0.8754 | 0.8405 | 0.8413 | 0.8080 | 0.8105 | 0.8217 |
| 20% | 0.9374 | 0.9100 | 0.8979 | 0.9308 | 0.8862 | 0.8875 |

# 7. Analysis of Two-Factor Designs

In this chapter, the results from Chapter 4 are extended to designs involving two factors. The focus of this chapter is to evaluate designs for a second order model which involves ME in $x_1$ only. The model is as follows:

$$y_i = \beta_0 + \beta_1 x_{1i} + \beta_2 x_{2i} + \beta_{12} x_{1i} x_{2i} + \beta_{11} x_{1i}^2 + \beta_{22} x_{2i}^2 + e_i, \quad i = 1, 2, ..., n, \qquad (7.1)$$
$$x_{1i} = X_{1i} + u_{1i},$$
$$e_i \sim N(0, 1),$$
$$u_{1i} \sim N(0, \sigma_1^2),$$

where var($y_i$) is a special case of equation (1.10),

$$\text{var}(y_i) = \sigma_0^2 + \sigma_1^2 [\beta_1 + \beta_{12} X_{2i} + 2\beta_{11} X_{1i}]^2 + 2\beta_{11}^2 \sigma_1^4. \qquad (7.2)$$

Notice that the variance is a function of all coefficients for model terms involving $X_1$, the design factor containing ME.

## 7.1 Simulation Details

The correct analysis for this type of data is presented for a k-factor model in Section 1 of Chapter 4, so the reader should refer to that section for details of the analysis. The correct analysis of the data will be compared to the OLS analysis as in Chapter 4. Performance results for the two analyses based on ME magnitude will be presented in this chapter.

The design used in the simulations was an eleven-point CCD with three center runs and the value of the axial point at ±2. The simulations included 2500 data sets for each design situation. The magnitude of the ME was varied so that the standard deviation of the ME was between 2.5% and 20% of the range of $X_1$. Coefficient combinations were varied as well.

There are six model coefficients for the full second order model. For this reason, many different coefficient combinations were considered in the comparison. However, only a few of these combinations appear in the summary figures, because many of the combinations have very similar results when comparing the two analysis methods.

The coefficient combinations are listed in the legend for each figure. The vector of numbers for each entry in the legend represent $\{\beta_1, \beta_2, \beta_{12}, \beta_{11}, \beta_{22}\}$. The plotted values represent the proportion of efficiency gained by analyzing the data using the IRWLS analysis described in Chapter 4 instead of the typical OLS analysis.

## 7.2 Results and Conclusions

The effect of ME on the estimation of $\beta_1$, $\beta_{11}$, and $\beta_{12}$ is summarized in Figure 7.1 - Figure 7.3. The most interesting effect which is apparent in all three figures is the leveling off in performance of the IRWLS analysis after ME reaches a certain magnitude. Notice that for almost all coefficient combinations, the relative improvement gained by using the IRWLS analysis stabilizes or declines after the ME magnitude reaches 15-17.5% of the range of *X*. Note that this is the relative improvement, so the absolute variances of the IRWLS coefficients are still smaller than the OLS variances of coefficients.

There is quite a difference in the performance of the IRWLS analysis based on the coefficients of the true model. At a ME magnitude of 10% of the range of $X_1$, the amount of improvement varies greatly for $\beta_1$ (2.5% to 32%), $\beta_{11}$ (7% to 23%) and $\beta_{12}$ (8% to 26%). However, it is interesting that the level of improvement is different across the coefficient variances for the same set of true model coefficients. For example, consider the true coefficient vector $\underline{\beta}'$ = {1,3,1,1,1,1}. At a ME magnitude of 10% of the range of $X_1$, the improvement for the IRWLS procedure is only 4% for $\beta_1$, but the improvement is 20% for $\beta_{11}$ and 24% for $\beta_{12}$. For the coefficient vector $\underline{\beta}'$ = {1,1,1,1,3,1}, the improvement is 32% for $\beta_1$ and 23% for $\beta_{11}$, but it is only 10% for $\beta_{12}$. This result seems to suggest that the improvement in estimation of an individual coefficient must be considered in relation to the estimation of other coefficients.

In general, the IRWLS analysis improves upon the OLS analysis by 15-30% when a ME magnitude reaches 10% or more of the range of *X*.

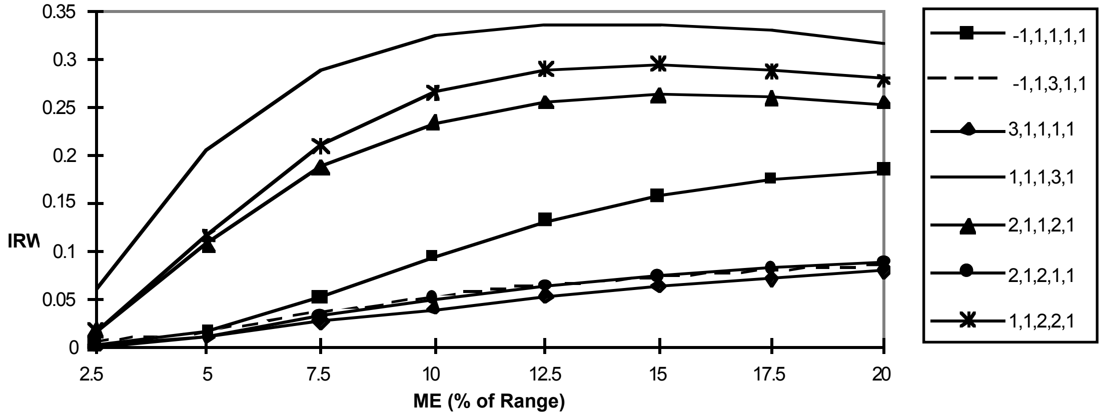


Figure 7.1 Improvement of IRWLS Analysis over OLS Analysis—Estimation of $\beta_1$

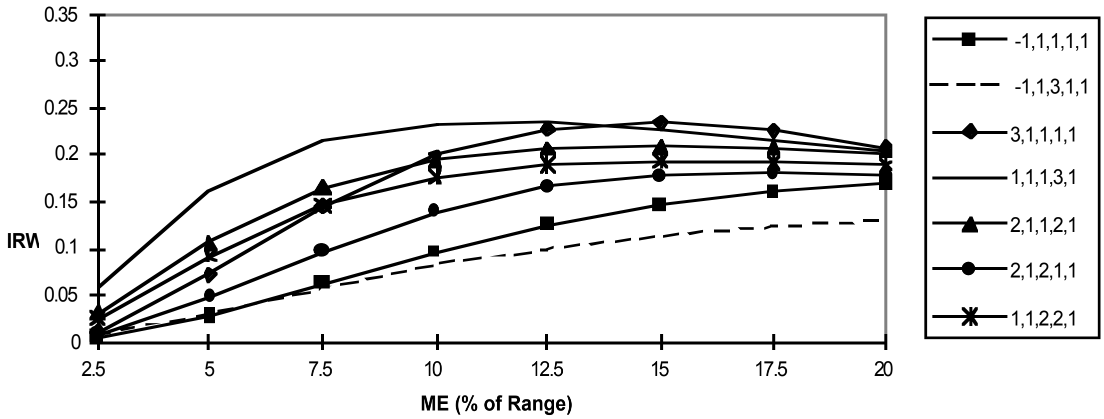


Figure 7.2 Improvement of IRWLS Analysis over OLS Analysis—Estimation of $\beta_{11}$

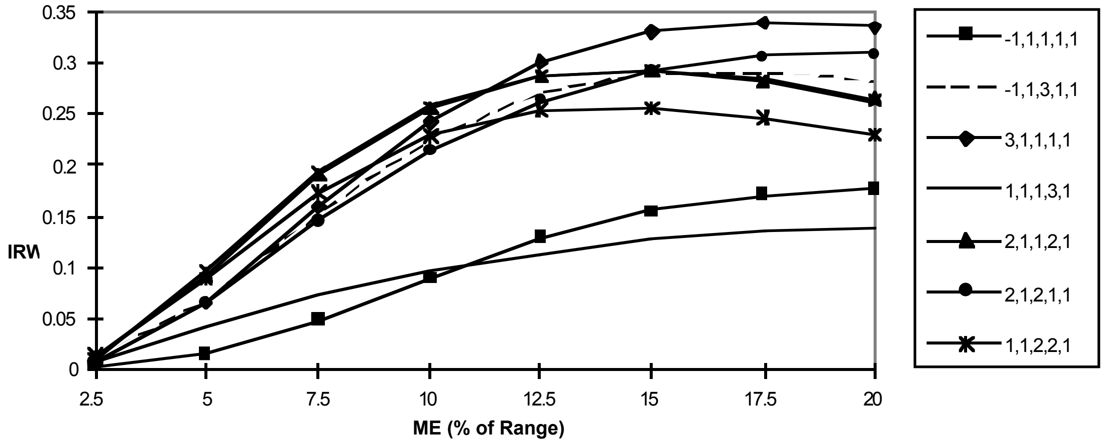


Figure 7.3 Improvement of IRWLS Analysis over OLS Analysis—Estimation of $\beta_{12}$

# 8. Two-Factor Results for the $D_{ME}$ Criterion

The $D_{ME}$ criterion for designs to estimate second order models is developed in Chapter 6. The performance of the criterion is evaluated for single-factor designs. However, the development of the criterion in Chapter 6 is for a more general k-factor design situation, providing that only a single variable contains ME. In this chapter, the performance of the $D_{ME}$ design criterion will be explored for designs with two factors. The model used for the data is presented in equation (7.1).

This chapter also includes a comprehensive comparison of design methods accounting for ME in the design factor versus design methods ignoring ME. Method 1, which accounts for ME, will include an initial design which is augmented by the $D_{ME}$ criterion method. The resulting data set will be analyzed using the IRWLS procedure outlined in Chapter 4. Method 2 will ignore ME in the design factor, and the same initial data set used in Method 1 will be augmented using the D-optimality criterion. The design data from this procedure will be analyzed using OLS analysis. An example from the semiconductor industry will illustrate the differences in the designs and resulting estimated models.

## 8.1 Two Factor Design Details

Two different design augmentations are considered. Both situations include an eleven-point CCD for the initial design. The CCD has three center runs and axial points at ±2 for both factors. Candidate points are all combinations of points between -2 and 2 at intervals of 0.5 for both factors. The grid of candidate points is less dense than for the single factor augmentation procedure presented in Chapter 6. However, a simulation using a finer grid of candidate points (points between -2 and 2 at intervals of 0.10) showed little difference from the larger grid in terms of design efficiency.

The two designs considered here differ in the number of points in the second stage of the design. Design 1 is augmented to 22 points, while Design 2 is augmented to 30 points. The standard deviation of the ME ranges from 5-20% of the range of $X$. As usual, several coefficient combinations are considered. The D-optimal second stage designs appear in Table 8.1. Design efficiencies are calculated as

$$D/D_{ME} \text{ efficiency} = \left[ \frac{\left| (X^{*\prime}V^{-1}X^{*})^{-1}_{D_{ME}} \right|}{\left| (X^{*\prime}V^{-1}X^{*})^{-1}_{D} \right|} \right]^{1/6} . \qquad (8.1)$$

Efficiency results appear in Table 8.2. The efficiencies show a slight improvement when using a $D_{ME}$ design rather than a D-optimal design. The improvement is more apparent for a two-factor design than for the single factor design presented in Chapter 6. However, there is little evidence to support the use of the $D_{ME}$ criterion for augmenting an initial design. This is especially true if the experimenter intends to account for the ME in the data analysis.

Although the improvement in efficiency may be negligible, there are other reasons that the $D_{ME}$-optimal design may be more attractive than the D-optimal design. The example in Section 8.3 demonstrates the difference in the second stage designs for the two criteria (D and $D_{ME}$). The design based on the $D_{ME}$ criterion is unique and more intuitive than the design based on the D criterion. In many cases, there are several design augmentations which may have the same D-efficiency. The choice of the best design is then arbitrary. A unique design which accounts for ME is more appealing than one design of several which does not account for ME.

Table 8.1 D-optimal Second Stage Designs

| Design | D-optimal Second Stage Design ($X_1$, $X_2$) |
|---|---|
| Design 1 (22 points) | (2,2), (2,2), (2,-2), (2,-2), (2,-2), (-2,2), (-2,2), (-2,2), (-2,-2), (-2,-2), (-2,-2) |
| Design 2 (30 points) | (2,2), (2,2), (2,2), (2,2), (2,-2), (2,-2), (2,-2), (2,-2), (-2,2), (-2,2), (-2,2), (-2,2), (-2,-2), (-2,-2), (-2,-2), (-2,-2),(0,-2), (0,2), (2,0) |

Table 8.2 Design Efficiencies for D-optimal vs. $D_{ME}$ Designs: Two Factors

| Design 1 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ($\beta_1$, $\beta_2$, $\beta_{12}$, $\beta_{11}$, $\beta_{22}$) | (2,1,2,1,1) | (2,2,1,2,1) | (3,1,1,1,1) | (2,1,1,-2,1) | (1,1,1,3,1) | (2,2,2,-2,-2) | (1,1,3,1,1) |
| ME (% of Range) | | | | | | | |
| 5% | 0.9921 | 0.9552 | 0.9886 | 0.9447 | 0.9305 | 0.9558 | 0.9825 |
| 10% | 0.9604 | 0.9094 | 0.9605 | 0.8959 | 0.8884 | 0.9135 | 0.9497 |
| 15% | 0.9441 | 0.9097 | 0.9517 | 0.8961 | 0.9015 | 0.9097 | 0.9325 |
| 20% | 0.9447 | 0.9273 | 0.9553 | 0.9135 | 0.9254 | 0.9218 | 0.9365 |
| Design 2 | | | | | | | |
| ($\beta_1$, $\beta_2$, $\beta_{12}$, $\beta_{11}$, $\beta_{22}$) | (2,1,2,1,1) | (2,2,1,2,1) | (3,1,1,1,1) | (2,1,1,-2,1) | (1,1,1,3,1) | (2,2,2,-2,-2) | (1,1,3,1,1) |
| ME (% of Range) | | | | | | | |
| 5% | 0.9848 | 0.9776 | 0.9941 | 0.9677 | 0.9446 | 0.9647 | 0.9776 |
| 10% | 0.9560 | 0.9312 | 0.9681 | 0.9221 | 0.9025 | 0.9266 | 0.9347 |
| 15% | 0.9394 | 0.9266 | 0.9569 | 0.9171 | 0.9140 | 0.9203 | 0.9127 |
| 20% | 0.9367 | 0.9425 | 0.9571 | 0.9347 | 0.9366 | 0.9326 | 0.9116 |

## 8.2 Accounting for ME: A Method Comparison

The work in this section evaluates the $D_{ME}$ design criterion by comparing it to a design and analysis method which completely ignore ME. This comparison is valid because most practitioners would ignore ME in the analysis of experimental data as well as the planning stages of the design. This design situation involves ME in the design factor $X_1$. For Method 1, the case accounting for ME in $X_1$, a $D_{ME}$ optimal design will be created based on an initial design. The data will be analyzed using the appropriate IRWLS analysis. For Method 2, the naïve case, a D-optimal second stage design will be added to an initial design. The resulting data set will be analyzed using OLS analysis. Efficiencies for these procedures will be calculated as

$$\text{Total Efficiency} = \left[\frac{\left|(X^{*\prime}V^{-1}X^{*})^{-1}_{D_{ME}}\right|}{\left|(X'X)^{-1}_{D}\cdot\bar{s}^{2}\right|}\right]^{1/6}, \qquad (8.2)$$

where $\bar{s}^2$ is the average MSE for the data sets created by the D-optimal design. Efficiencies appear in Table 8.3. When both design and analysis are combined into a total ME method, it is apparent that the efficiency of the method is much greater than the design/analysis method ignoring ME, especially for ME standard deviations of 10% of the range of $X_1$ or more.

Table 8.3 Total Efficiencies for D-optimal vs. $D_{ME}$ Designs: Two Factors

| Design 1 | | | | | | | |
|---|---|---|---|---|---|---|---|
| ($\beta_1$, $\beta_2$, $\beta_{12}$, $\beta_{11}$, $\beta_{22}$) | (2,1,2,1,1) | (2,2,1,2,1) | (3,1,1,1,1) | (2,1,1,-2,1) | (1,1,1,3,1) | (2,2,2,-2,-2) | (1,1,3,1,1) |
| ME (% of Range) | | | | | | | |
| 5% | 0.9344 | 0.8685 | 0.9279 | 0.7894 | 0.7494 | 0.7318 | 0.8920 |
| 10% | 0.7215 | 0.6685 | 0.7112 | 0.5912 | 0.5617 | 0.5303 | 0.6542 |
| 15% | 0.6454 | 0.6371 | 0.6130 | 0.5486 | 0.5768 | 0.4871 | 0.5606 |
| 20% | 0.6083 | 0.6731 | 0.5731 | 0.5790 | 0.6484 | 0.5102 | 0.5242 |
| Design 2 | | | | | | | |
| ($\beta_1$, $\beta_2$, $\beta_{12}$, $\beta_{11}$, $\beta_{22}$) | (2,1,2,1,1) | (2,2,1,2,1) | (3,1,1,1,1) | (2,1,1,-2,1) | (1,1,1,3,1) | (2,2,2,-2,-2) | (1,1,3,1,1) |
| ME (% of Range) | | | | | | | |
| 5% | 0.8465 | 0.8211 | 0.8772 | 0.7957 | 0.7062 | 0.73225 | 0.8049 |
| 10% | 0.6103 | 0.6087 | 0.6373 | 0.5822 | 0.5150 | 0.5204 | 0.5507 |
| 15% | 0.5107 | 0.5624 | 0.5151 | 0.5425 | 0.5240 | 0.4826 | 0.4499 |
| 20% | 0.4850 | 0.5972 | 0.4855 | 0.5866 | 0.5938 | 0.5255 | 0.4230 |

In the following section, an example from the semiconductor industry is presented. The data in the example are simulated, but the experimental goals outlined in the discussion are relevant to the manufacturing processes in the industry. The example will illustrate the performance of the ME methodology developed in this dissertation. The performance will be compared to a design plan and analysis which ignore the ME.

## 8.3 Example

The creation of a semiconductor is a very complex process. Semiconductors are composed of numerous layers of different chemicals. Each layer contains a maze-like pattern which directs the flow of electrons. These layers are "built" sequentially on top of a disc made of pure silicon, called a *wafer*. There are many individual semiconductors, each of which is called a *die*, on a wafer which has completed all process steps. Process improvement teams constantly strive to increase the die *yield* of a wafer, which is a measure of the number of functioning die on a completed wafer.

At each step in the manufacturing process, there are parameters which are directly related to the die yield of a wafer. Because of the extremely small dimensions of the pattern on a layer, the specifications for the thickness of each layer are very precise and important. A thickness measurement, measured in angstroms ($\mathring{A}$), is recorded after every layer is deposited or grown onto the wafer. It is essential that the layer thickness is correct for each die on the wafer, so thickness *uniformity* across the wafer is also an important measure for each layer. Uniformity is often measured as the absolute difference in thickness at wafer center and thickness at wafer edge ($|\mathring{A}_c - \mathring{A}_e|$).

The response surface experiment in this example focuses on minimizing the uniformity of the silicon dioxide ($SiO_2$) layer. $SiO_2$ is grown by diffusing oxygen into the bare silicon wafer. This process takes place inside a diffusion furnace. Extremely high temperatures (around 1000$^o$ C) and relatively long periods of time (10-12 hours) are required for the successful growth of a layer.

Length of time inside the diffusion furnace and sustained temperature inside the furnace are experimental factors which greatly influence the uniformity of the $SiO_2$ layer thickness. Information from previous experiments indicates that data from this system follow a second order model. Previous process characterization has provided information about ranges for time and temperature.

For a certain thickness of the $SiO_2$ layer, the length of time a wafer must remain inside the diffusion furnace is known to be between 570 and 690 minutes. The current temperature for the process is 1100$^o$ C, but the experimental range for the process is between 960$^o$ C and 1240$^o$ C. The processing time can be controlled exactly for the purposes of experimentation. However, the temperature cannot be controlled completely in the manufacturing setting. Many wafers are processed simultaneously within a large furnace. The size of the diffusion furnace causes a slight variation in temperature across the group of wafers in the same process step, so that the sustained temperature for a typical wafer is within the interval $1100 \pm 42^o$ C.

The initial nine-point design is a CCD with axial points at ±2 and a single center run (see Table 1.1). The design points in coded and natural units appear in Table 8.4. For each experimental run, a randomly chosen wafer was measured for uniformity. The responses are included in Table 8.4 as $y_1$. Fortunately, production schedules allowed for an additional nine design runs, so an augmentation procedure was required. Because the temperature factor could not be controlled completely, a $D_{ME}$ design augmentation procedure was chosen. The design was augmented according to the methodology outlined in Section 6.4.1, using the coefficient estimates from the initial design and a ME standard deviation of 42 (15% of the range). The candidate points included all values between -2 and 2 in 0.10 increments. The resulting second-stage design is presented in

Table 8.5. It is evident that this design differs greatly from a typical D-optimal design, because several design points occur in the interior of the design. For a D-optimal design, augmented points are almost always at the design edges, with an occasional augmented design point at the design center.

Results for the experiment involving the $D_{ME}$ augmentation were then compared to a separate experiment which ignored ME in the temperature factor. The same initial design was used, and the responses appear in Table 8.4 as $y_2$. Based on the initial design, the DETMAX (Mitchell, 1974) algorithm was used to create a D-optimal nine-point augmentation. The second stage design points and responses are summarized in Table 8.5.

Table 8.4 Example: Initial Design Points and Responses

| $X_1$ (coded) | $X_1$ ($^o$ C ) | $X_2$ (coded) | $X_2$ (min) | $y_1$ ($D_{ME}$ ) | $y_2$ (D ) |
|---|---|---|---|---|---|
| -2 | 570 | 0 | 1100 | 103.37 | 90.41 |
| -1 | 600 | -1 | 1030 | 53.04 | 42.38 |
| -1 | 600 | 1 | 1170 | 62.28 | 85.76 |
| 0 | 630 | -2 | 960 | 66.73 | 80.22 |
| 0 | 630 | 0 | 1100 | 35.02 | 37.43 |
| 0 | 630 | 2 | 1240 | 43.47 | 45.85 |
| 1 | 660 | -1 | 1030 | 63.25 | 70.68 |
| 1 | 660 | 1 | 1170 | 35.69 | 37.78 |
| 2 | 690 | 0 | 1100 | 70.41 | 50.85 |

Table 8.5 Example: Second Stage Design Points and Responses

| $D_{ME}$ design (coded) | $D_{ME}$ design (°C, min) | $y_1$ | D design (coded) | D design (°C, min) | $y_2$ |
|---|---|---|---|---|---|
| ( 1.1, 2) | (663, 1240) | 46.20 | (-2, -2) | (570, 960) | 107.18 |
| (-1.1, -2) | (597, 960) | 66.64 | (-2, -2) | (570, 960) | 89.46 |
| ( 2, 2) | (690, 1240) | 72.50 | (-2, -2) | (570, 960) | 96.62 |
| ( 2, -2) | (690, 960) | 150.01 | (-2, 2) | (570, 1240) | 112.94 |
| (-2, -2) | (570, 960) | 105.26 | (-2, 2) | (570, 1240) | 116.79 |
| (-2, 2) | (570, 1240) | 157.52 | (2, -2) | (690, 960) | 113.92 |
| (-0.5, -2) | (615, 960) | 64.75 | (2, -2) | (690, 960) | 110.69 |
| (0.9, 2) | (657, 1240) | 45.90 | (2, 2) | (690, 1240) | 56.73 |
| (0.2, 0) | (636, 1100) | 32.66 | (2, 2) | (690, 1240) | 59.71 |

After completing both experiments, the results were analyzed. The data from the design created by the $D_{ME}$ criterion was analyzed using IRWLS analysis, while the results from the D criterion were analyzed using OLS analysis. Table 8.6 presents the true model used to simulate the data and the model coefficient estimates from the two analyses. The true minimum uniformity (29.63 Å) occurs at $\{X_1, X_2\} = \{0.38, 0.47\}$, or 1126.6° C and 644.1 minutes. The predicted minimum for the $D_{ME}$ data is 31.47 Å, and it occurs at {0.27, 0.50}={1118.9° C, 645 minutes}. The predicted minimum for the D-optimal data is 39.15 Å, and it occurs at {0.62,0.68}={1143.4° C, 650.4 minutes}.

Table 8.6 True and Estimated Models for Two-Factor Experiment

| True Model | $\beta_0$ | $\beta_1$ | $\beta_2$ | $\beta_{12}$ | $\beta_{11}$ | $\beta_{22}$ | $\sigma_0$ |
|---|---|---|---|---|---|---|---|
| | 31.5 | -4.72 | -4.14 | -6.8 | 10.44 | 7.13 | 2 |
| Estimated Models | $b_0$ | $b_1$ | $b_2$ | $b_{12}$ | $b_{11}$ | $b_{22}$ | $s_0$ |
| $D_{ME}$ design | 33.05 | -4.06 | -4.12 | -7.78 | 14.79 | 6.18 | – |
| D-opt design | 42.63 | -6.08 | -4.69 | -4.89 | 7.58 | 5.68 | 11.5 |

Contour plots of the true and estimated surfaces are shown in Figure 8.1 - Figure 8.3. It is evident that the contours of the estimated surface from the ME methods are much closer to the true surface than the contours of the naïve method. Augmented designs for the two methods are superimposed over the true surface in Figure 8.4 and Figure 8.5. The figures show that the design augmentation of the naïve method ignores the true surface, placing points at the edge of the design. The design augmentation for the ME method places points on the *interior of the design for* $X_1$, which is the variable containing ME. Note also that the points are placed in areas where the contours are less steep. This result corresponds to placing the points in areas of smaller variance. To see the connection between flatter contours and smaller variance, consider the variance expression in equation 7.2. The relationship between the coefficient magnitudes and the variance magnitudes is apparent. A final point for the design is placed near the center, but slightly in the direction of the minimum.

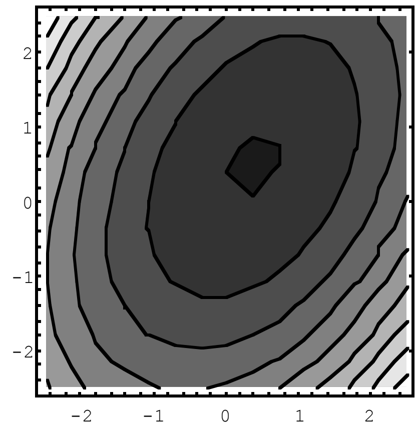


Figure 8.1 Contour Plot of True Response Surface

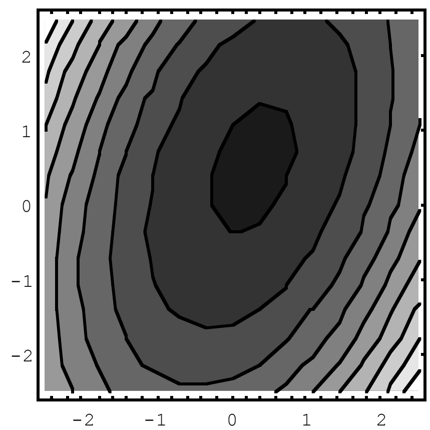


Figure 8.2 Contour Plot of the Estimated Surface ($D_{ME}$ Design, IRWLS Analysis)

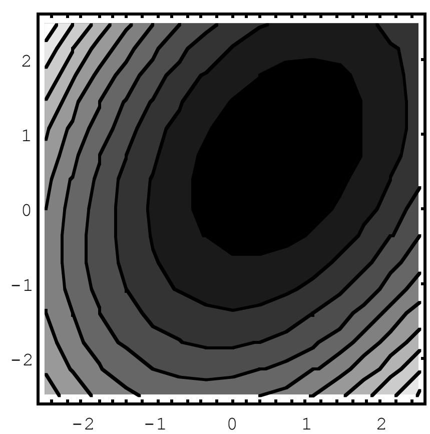


Figure 8.3 Contour Plot of the Estimated Surface (D-optimal Design, OLS Analysis)

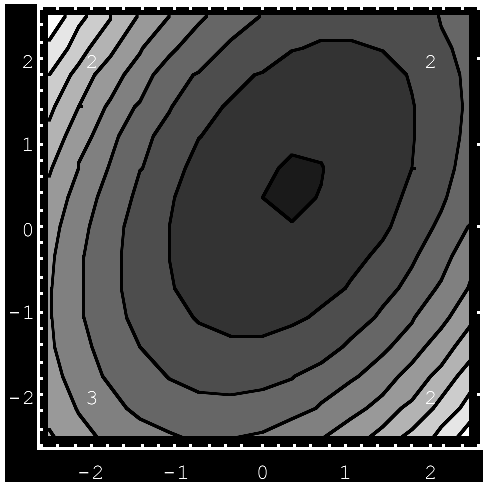


Figure 8.4 Augmented Design for Naïve Method
(Value indicates number of points at each new design point)

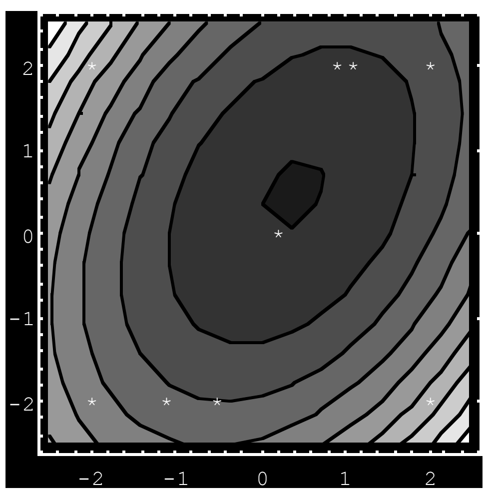


Figure 8.5  Augmented Design for ME Method
(A * indicates the new design point)

# 9. Future Research

## 9.1 Analysis Issues

One assumption of this research is that the ME variance for the affected design factor is a known value. This assumption is idealistic, as assumptions often are. Creating an unbiased estimate for the ME variance is a straightforward problem. However, the parameter $\sigma_1^2$ appears in the modified model matrix for the IRWLS analysis. Replacing this parameter with an estimate in the model matrix complicates the properties of the IRWLS analysis. These theoretical properties need to be developed. Another approach to the ME variance problem might be a Bayesian analysis which assumes a prior distribution on the ME variance.

Another area of interest is modification of the initial weights appearing in the IRWLS analysis. Recall that the weights have the form in equation 4.6. Replacing the model variance $\sigma_0^2$ with the MSE from an OLS analysis actually inflates these weights. This is true because $E(MSE_{ols}) > \sigma_0^2$, even in the first order case. The MSE from an OLS analysis represents the average variance across the design, rather than the error in *y* which is unexplained by the model. A better estimate for $\sigma_0^2$ could improve the initial weights for the IRWLS analysis. This may also create average estimated variances for $\underline{\beta}_{IRWLS}$ which are much closer to the true variances observed through simulation. This improvement would increase the appeal of the IRWLS analysis to practitioners, since the current analysis yields inflated variance estimates for the coefficients.

## 9.2 Design Issues

Investigation into the $D_{ME}$ design efficiency for designs with more than 2 factors is also of interest. The efficiencies for one- and two factor designs were not impressive, but the improvement in efficiency from one to two factors was evident. Note that as the design space increases in dimension, the var($y_i$) for a full second order model becomes more complex across that region. In other words, more of the coefficient terms appear in the variance expression and so the variance is more dependent on the true response surface.  Perhaps this could increase the performance of design criterion accounting for ME in a design factor.

The results in this dissertation refer to designs in which only one design factor contains ME.  Outlining results for designs with ME in more than one factor would be another natural extension of this research.

Another possibility is to create other design criteria for designs involving ME.  One example is a criterion which minimizes the variance of $y_i$ across the design.  The results of the example in Section 8.3 suggest that the $D_{ME}$ augmentation procedure places points where the contours of the response surface are shallow.  If simply minimizing the slope of the response surface is used as a criterion, then information about the ME magnitude is not required.

## 9.3 Model Issues

The results in this dissertation refer to a specific model for ME.  Other models for ME in designed experiments may be more relevant in certain disciplines.  Exploration into properties for these models, especially for the first order case, is an appropriate avenue of further research for ME in designed experiments.

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# Appendix

## Appendix A

### Contrasts for Two Factor CCDs

For the two factor CCD with axial points at $d$ and $-d$ and $n_c$ center runs , the general expressions for orthogonal contrasts representing model effect estimates follow. They are presented using the notation of Chapter 2.

$\underline{1}' = \{ 1, 1, 1, 1, 1, 1, 1, 1, n_c\}$,
$\underline{x}_1' = \{-1,-1, 1, 1, d,-d, 0, 0, \underline{0}'_{1 \times nc}\}$,
$\underline{x}_2' = \{-1, 1,-1, 1, 0, 0, d,-d, \underline{0}'_{1 \times nc}\}$,

$\underline{\alpha}^*(\beta_0) = [B]^{-1/2}\ \underline{1}$,
$\underline{\alpha}^*(\beta_1) = [A]^{-1/2}\ \underline{x}_1$,
$\underline{\alpha}^*(\beta_2) = [A]^{-1/2}\ \underline{x}_2$,
$\underline{\alpha}^*(\beta_{12}) = [1/2]\ \underline{x_1\ x_2}$,
$\underline{\alpha}^*(\beta_{11}) = [(2C)/B]^{-1/2}\ [\underline{x}_1^2 - (A/B)\underline{1}]$, and
$\underline{\alpha}^*(\beta_{22}) = [(2Dd^4)/C]^{-1/2}\ [\underline{x}_2^2 - (E/C)\ \underline{x}_1^2 + ((A/B)(E/C - 1))\underline{1}]$,

where $A = 4 + 2d^2$,
$B = 8 + n_c^2$,
$C = (8 - 8d^2 + 6d^4 + 2n_c^2 + d^4 n_c^2)$,
$D = 16 - 16d^2 + 4d^4 + 4n_c^2 + d^4 n_c^2$, and
$E = 2(4 - 4d^2 - d^4 + n_c^2)$.

The residual effects may be written similarly. The residual effect coefficients ($\underline{\alpha}_g$) for a two factor CCD are as follows:

$\underline{\alpha}_1 = [8d^2/A]^{-1/2}\ [\underline{x_1^2\ x_2} - (4/A)\ \underline{x}_2]$,
$\underline{\alpha}_2 = [8d^2/A]^{-1/2}\ [\underline{x_1\ x_2^2} - (4/A)\ \underline{x}_1]$, and

$\underline{\alpha_3}$ = $[(4d^4 n_c^{\ 2})/D]^{-1/2}$ $[\underline{x_1}^2 \underline{x_2}^2 + ((E + d^2A)/C)(E/D - 1)\ \underline{x_1}^2 - ((E + d^2A)/D)\ \underline{x_2}^2 + \{((E + d^2A)/D)(A/B) + (((E + d^2A)/C)(A/B)(1 - E/D)) - (4/B)\}\underline{1}]$.

If the axial point values are allowed to differ for the two factors and only a single center run is included, the effect contrasts may be written as follows:

$\underline{\alpha}*(\beta_0) = [9]^{-1/2}\ \underline{1}$,
$\underline{\alpha}*(\beta_1) = [4 + 2d1^2]^{-1/2}\ \underline{x_1}$,
$\underline{\alpha}*(\beta_2) = [4 + 2d2^2]^{-1/2}\ \underline{x_2}$,
$\underline{\alpha}*(\beta_{12}) = [1/2]\ \underline{x_1}\ \underline{x_2}$,
$\underline{\alpha}*(\beta_{11}) = [(2A_1)/9]^{-1/2}\ [\underline{x_1}^2 - ((4 + d1^2)/9)\underline{1}]$, and
$\underline{\alpha}*(\beta_{22}) = [(2B_1)/A_1]^{-1/2}\ [\underline{x_2}^2 - ((-10 + 4d1^2 + 4d2^2 + 2d1^2d2^2)/A_1)\ \underline{x_1}^2 + ((4d1^2 + 4d1^4 - 4d2^2 - d1^4d2^2)/A_1)\underline{1}]$,

where
$A_1 = 10 - 8d1^2 + 14d1^4$, and
$B_1 = 6d1^4 + 8d1^2d2^2 - 8d1^4d2^2 + 6d2^4 - 8d1^2d2^4 + 5d1^4d2^4$.
The corresponding residual effects are

$\underline{\alpha_1} = [8d2^2/(4 + 2d2^2)]^{-1/2}\ [\underline{x_1}^2 \underline{x_2} - (4/(4 + 2d2^2))\ \underline{x_2}]$,
$\underline{\alpha_2} = [8d1^2/(4 + 2d1^2)]^{-1/2}\ [\underline{x_1}^2 \underline{x_2} - (4/(4 + 2d1^2))\ \underline{x_2}]$, and
$\underline{\alpha_3} = [(4d1^4\ d2^4)/B_1]^{-1/2}\ [\underline{x_1}^2 \underline{x_2}^2 + ((2d2^2(-2d1^2 - 3d2^2 + 2d1^2d2^2))/B_1)\ \underline{x_1}^2 - ((2d1^2(-3d1^2 - 2d2^2 + 2d1^2d2^2))/B_1)\underline{x_2}^2 + ((4d1^2d2^2(d1^2 + d2^2 - d1^2d2^2))/B_1)\underline{1}]$.

Appendix B

Contrasts for Three Factor CCDs

For the three factor CCD with axial points at $d$ and $-d$ and a single center run, general expressions for orthogonal contrasts representing model effect estimates are presented using the notation of Section 4.

$\underline{1}' = \{ 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1\}$,
$\underline{x}_1' = \{-1,-1,-1,-1, 1, 1, 1, 1, d,-d, 0, 0, 0, 0, 0\}$,
$\underline{x}_2' = \{-1,-1, 1, 1,-1,-1, 1, 1, 0, 0, d,-d, 0, 0, 0\}$,
$\underline{x}_3' = \{-1, 1,-1, 1,-1, 1,-1, 1, 0, 0, 0, 0, d,-d, 0\}$,

$\underline{\alpha}^*(\beta_0) = [15]^{-1/2}\ \underline{1}$
$\underline{\alpha}^*(\beta_1) = [8 + 2d^2]^{-1/2}\ \underline{x}_1$
$\underline{\alpha}^*(\beta_2) = [8 + 2d^2]^{-1/2}\ \underline{x}_2$
$\underline{\alpha}^*(\beta_3) = [8 + 2d^2]^{-1/2}\ \underline{x}_3$
$\underline{\alpha}^*(\beta_{12}) = [8]^{-1/2}\ \underline{x}_1\,\underline{x}_2$
$\underline{\alpha}^*(\beta_{13}) = [8]^{-1/2}\ \underline{x}_1\,\underline{x}_3$
$\underline{\alpha}^*(\beta_{23}) = [8]^{-1/2}\ \underline{x}_2\,\underline{x}_3$

$$\underline{\alpha}^*(\beta_{11}) = [\frac{2(28-16d^2+13d^4)}{15}]^{-1/2}\ [\underline{x}_1^{\,2} - (\frac{8+2d^2}{15})\underline{1}]$$

$$\underline{\alpha}^*(\beta_{22}) = [\frac{2d^4(56-32d^2+11d^4)}{28-16d^2+13d^4}]^{-1/2}\ [\underline{x}_2^{\,2} - ((\frac{28-16d^2-2d^4}{28-16d^2+13d^4})[\underline{x}_1^{\,2} - (\frac{8+2d^2}{15})\underline{1}]) + (\frac{8+2d^2}{15})\underline{1}]$$

$$\underline{\alpha}^*(\beta_{33}) = [\frac{6d^4(28-16d^2+3d^4)}{56-32d^2+11^4}]^{-1/2} [\underline{x}_3^2 - \{(\frac{28-16d^2-2d^4}{28-16d^2+13d^4})[\underline{x}_1^2 - (\frac{8+2d^2}{15})\underline{1}]\} -$$

$$\{(\frac{28-16d^2-2d^4}{56-32d^2+11^4})\{\underline{x}_2^2 - ((\frac{28-16d^2-2d^4}{28-16d^2+13d^4})[\underline{x}_1^2 - (\frac{8+2d^2}{15})\underline{1}]) + (\frac{8+2d^2}{15})\underline{1}\}\} -$$

$$(\frac{8+2d^2}{15})\underline{1}]$$

The corresponding residual effects are

$$\underline{\alpha}_1 = \underline{\alpha}^*(\beta_{123}) = [8]^{-1/2}\, \underline{x}_1\, \underline{x}_2\, \underline{x}_3$$

$$\underline{\alpha}_2 = \underline{\alpha}^*(\beta_{122}) = [\frac{16d^2}{8+2d^2}]^{-1/2}[\underline{x}_1\, \underline{x}_2\, \underline{x}_2 - (\frac{8}{8+2d^2})\underline{x}_1]$$

$$\underline{\alpha}_3 = \underline{\alpha}^*(\beta_{233}) = [\frac{16d^2}{8+2d^2}]^{-1/2}[\underline{x}_2\, \underline{x}_3\, \underline{x}_3 - (\frac{8}{8+2d^2})\underline{x}_2]$$

$$\underline{\alpha}_4 = \underline{\alpha}^*(\beta_{333}) = [\frac{16d^2(d^2-1)^2}{8+2d^2}]^{-1/2}[\underline{x}_3\, \underline{x}_3\, \underline{x}_3 - (\frac{8+2d^4}{8+2d^2})\underline{x}_3]$$

$$\underline{\alpha}_5 = \underline{\alpha}^*(\beta_{1133}) = [\frac{8d^2}{3(28-16d^2+3d^4)}]^{-1/2} [\underline{x}_1\, \underline{x}_1\, \underline{x}_3\, \underline{x}_3 + (\frac{8d^4-28}{28-16d^2+13d^4})\underline{\ \ }\underline{x}_1^2 +$$

$$(\frac{8d^4-28}{56-32d^2+11d^4})\underline{x}_2^2 + (\frac{8d^4-28}{84-48d^2+9d^4})\underline{x}_3^2 - (\frac{8}{15})\, \underline{1}\,]$$

Appendix C

The tables below contain the optimal values for axial points based on the true model and a particular contrast of interest. In a few cases, two values are listed as optimal values. In these cases, the squared bias for the variance estimate of a particular contrast was the same for both values. Not all true models yield two optimal values for a contrast, since the bias was minimized on a certain interval of sensible values for the axial points.

Table 1.1 2 Factor Optimal Values for Axial Point (Common Value for Both Factors)

| True Values | Contrast for Coefficient $\beta_i$ | | | |
|---|---|---|---|---|
| $\beta_{12}/\beta_{11}$ | $\beta_1$ | $\beta_2$ | $\beta_{11}$ | $\beta_{22}$ |
| $\beta_{12} = 0$ | .97 | 1.2 | 2.2 | 2.6 |
| $\beta_{11} = 0$ | 1.4 | .78 | 1.5 | .09 |
| $\beta_{12}/\beta_{11} = 1$ | .97 | 1.5 | 2.1 | 0 |
| $\beta_{12}/\beta_{11} = 1/2$ | .97 | 1.3 | 2.2 | 0 |
| $\beta_{12}/\beta_{11} = 1/3$ | .97 | 1.3 | 2.2 | 3.2 |
| $\beta_{12}/\beta_{11} = 1/4$ | .97 | 1.2 | 2.2 | 2.9 |
| $\beta_{12}/\beta_{11} = 2$ | .96 | .96 | 1.8 | 0 |
| $\beta_{12}/\beta_{11} = 3$ | 1.7 | .85 | 1.7 | 0 |
| $\beta_{12}/\beta_{11} = 4$ | 1.6 | .82 | 1.6 | 0 |

Table 1.2 2 Factor Optimal Values of Axial Point for $X1$ when $d2 = 1$

| True Values | Contrast for Coefficient $\beta_i$ | | | |
|---|---|---|---|---|
| $\beta_{12}/\beta_{11}$ | $\beta_1$ | $\beta_2$ | $\beta_{11}$ | $\beta_{22}$ |
| $\beta_{12} = 0$ | .97 | 1.2 | .78, 1.3 | .81, 1.3 |
| $\beta_{11} = 0$ | 1.1 | 4* | 1.1 | .67 |
| $\beta_{12}/\beta_{11} = 1$ | 1.1 | 1.4 | .83, 1.3 | .87, 1.2 |
| $\beta_{12}/\beta_{11} = 1/2$ | .99 | 1.2 | .79, 1.3 | .82, 1.3 |
| $\beta_{12}/\beta_{11} = 1/3$ | .98 | 1.2 | .78, 1.3 | .82, 1.3 |
| $\beta_{12}/\beta_{11} = 1/4$ | .98 | 1.2 | .78, 1.3 | .82, 1.3 |
| $\beta_{12}/\beta_{11} = 2$ | 1.2 | 1.7 | .94, 1.5 | .46 |
| $\beta_{12}/\beta_{11} = 3$ | 1.4 | 2.2 | 1, 1.8 | .6 |
| $\beta_{12}/\beta_{11} = 4$ | 1.3, 2 | 2.6 | 1, 2.2 | .63 |

*The squared bias expression is minimized as $d \to \infty$.

Table 1.3 2 Factor Optimal Values of Axial Point for $X1$ when $d2 = \sqrt{2}$

| True Values | Contrast for Coefficient $\beta_i$ | | | |
|---|---|---|---|---|
| $\beta_{12}/\beta_{11}$ | $\beta_1$ | $\beta_2$ | $\beta_{11}$ | $\beta_{22}$ |
| $\beta_{12} = 0$ | 1.1 | .76 | .71, 1.4 | 0 |
| $\beta_{11} = 0$ | .92 | 4* | 1.2 | .86 |
| $\beta_{12}/\beta_{11} = 1$ | 1.15 | .97 | .80, 1.4 | .12 |
| $\beta_{12}/\beta_{11} = 1/2$ | 1.1 | .82 | .73, 1.4 | 0 |
| $\beta_{12}/\beta_{11} = 1/3$ | 1.1 | .635 | .69, 1.4 | 0 |
| $\beta_{12}/\beta_{11} = 1/4$ | 1.1 | .61 | .69, 1.4 | 0 |
| $\beta_{12}/\beta_{11} = 2$ | 1.0, 1.5 | 4* | 1.1, 1.5 | .80 |
| $\beta_{12}/\beta_{11} = 3$ | .92, 1.9 | 4* | 1.3, 1.8 | .89, 2.1 |
| $\beta_{12}/\beta_{11} = 4$ | .88, 2.4 | 4* | 1.3, 2.2 | .93, 1.8 |

Table 2.1 3 Factor Optimal Values for Axial Point (Common Value for Both Factors)

| True Values | | | Contrast for Coefficient $\beta_i$ | | | | | |
|---|---|---|---|---|---|---|---|---|
| $\beta_{12}$ | $\beta_{13}$ | $\beta_{11}$ | $\beta_1$ | $\beta_2$ | $\beta_3$ | $\beta_{11}$ | $\beta_{22}$ | $\beta_{33}$ |
| 0 | 0 | 1 | 1.1 | 1.3 | 1.3 | .77 | .77 | .38,1.9 |
| 1 | 0 | 0 | 1.32 | 1.096 | 1.32 | 1.0 | 1.4 | .38,1.9 |
| 0 | 1 | 0 | 1.3 | 1.3 | 1.1 | 1.0 | 1.4 | .38, 1.9 |
| 1 | 1 | 1 | 1.45 | 1.4, 2.8 | 1.4, 2.8 | .84, 1.4 | .99, 2.7 | .36 |
| 1 | 1 | 2 | 1.2 | 1.35 | 1.35 | .79, 1.3 | .82, 1.1 | .37 |
| 1 | 1 | 3 | 1.1 | 1.3 | 1.3 | .78, 1.3 | .79, 1.1 | .37 |
| 1 | 1 | 4 | 1.1 | 1.3 | 1.3 | .78, 1.3 | .79 | .37 |
| 2 | 1 | 1 | 1.7 | 1.7 | 1.4, 3.6 | .90, 1.6 | 1.9 | .37 |
| 3 | 1 | 1 | 1.6, 2.0 | 1.5 | 1.4, 4.6 | .95, 1.9 | 1.7 | .37 |
| 4 | 1 | 1 | 1.5, 2.6 | 1.3 | 1.3 | .99, 2.3 | 1.6 | .37 |
| 1 | 2 | 1 | 1.6 | 1.4, 3.6 | 1.4, 3.6 | .90, 1.6 | 3.0 | .35 |
| 1 | 3 | 1 | 1.6, 2.0 | 1.4, 4.6 | 1.5 | .955, 1.9 | 3.4 | .34 |
| 1 | 4 | 1 | 1.5, 2.6 | 1.35 | 1.3 | .99, 2.3 | 3.9 | .34 |

Table 2.2 3 Factor Optimal Values of Axial Point for $X_1$ when $d2$=1

| True Values | | | Contrast for Coefficient $\beta_i$ | | | | | |
|---|---|---|---|---|---|---|---|---|
| $\beta_{12}$ | $\beta_{13}$ | $\beta_{11}$ | $\beta_1$ | $\beta_2$ | $\beta_3$ | $\beta_{11}$ | $\beta_{22}$ | $\beta_{33}$ |
| 0 | 0 | 1 | .95 | 2.0 | 2.0 | .72, 1.3 | .93, 1.7 | .96 |
| 1 | 0 | 0 | 1.7 | 6* | 6* | 1.0 | .79 | 1.3 |
| 0 | 1 | 0 | 1.7 | 6* | 6* | 1.04 | 1.434 | .8876 |
| 1 | 1 | 1 | 1.1 | 2.7 | 2.7 | .81, 1.3 | 1.0, 1.6 | 1.0 |
| 1 | 1 | 2 | .99 | 2.2 | 2.2 | .75, 1.3 | .96, 1.65 | .98 |
| 1 | 1 | 3 | .97 | 2.1 | 2.1 | .73, 1.3 | .94, 1.7 | .97 |
| 1 | 1 | 4 | .96 | 2.05 | 2.05 | .72, 1.3 | .94, 1.7 | .97 |
| 2 | 1 | 1 | 1.2 | 5.15 | 3.5 | .90, 1.4 | 1.3 | 1.3 |
| 3 | 1 | 1 | 1.4 | 6* | 5.3 | .96,1.6 | .54 | 1.55 |
| 4 | 1 | 1 | 1.7 | 6* | 6* | .99,1.95 | .67 | 1.7 |
| 1 | 2 | 1 | 1.2 | 3.5 | 5.15 | .895, 1.4 | 1.2, 1.7 | 0 |
| 1 | 3 | 1 | 1.4 | 5.3 | 6* | .96, 1.7 | 1.3, 1.9 | 0 |
| 1 | 4 | 1 | 1.7 | 6* | 6* | .99, 1.95 | 1.4, 2.2 | .66 |

* The squared bias expression is minimized as $d \to \infty$.

Table 2.3 3 Factor Optimal Values of Axial Point for $X_1$ when $d2 = \sqrt{3}$

| True Values | | | Contrast for Coefficient $\beta_i$ | | | | | |
|---|---|---|---|---|---|---|---|---|
| $\beta_{12}$ | $\beta_{13}$ | $\beta_{11}$ | $\beta_1$ | $\beta_2$ | $\beta_3$ | $\beta_{11}$ | $\beta_{22}$ | $\beta_{33}$ |
| 0 | 0 | 1 | 1.1 | .80 | .80 | .54,1.4 | 0 | .90 |
| 1 | 0 | 0 | .99 | 6* | 0 | 1.2 | 1.5 | 1.1 |
| 0 | 1 | 0 | .99 | 0 | 6* | 1.2 | 1.1, 1.5 | 1.2, 2.6 |
| 1 | 1 | 1 | 1.2 | 1.1 | 1.1 | .79, 1.5 | 0 | 0 |
| 1 | 1 | 2 | 1.1 | .91 | .91 | .615, 1.4 | 0 | .85 |
| 1 | 1 | 3 | 1.1 | .85 | .85 | .575, 1.4 | 0 | .88 |
| 1 | 1 | 4 | 1.1 | .83 | .83 | .56, 1.4 | 0 | .89 |
| 2 | 1 | 1 | 1.4 | 3.7 | .91 | .99, 1.6 | 1.2 | 0 |
| 3 | 1 | 1 | 1.2, 1.9 | 6* | .59 | 1.1, 1.95 | 1.7 | .94 |
| 4 | 1 | 1 | 1.1, 2.4 | 6* | 0 | 1.2, 2.4 | 1.6 | 1.0 |
| 1 | 2 | 1 | 1.4 | .91 | 3.7 | .99, 1.6 | 0 | .82 |
| 1 | 3 | 1 | 1.2, 1.9 | .59 | 6* | 1.1, 1.95 | 1.2 | 1.0 |
| 1 | 4 | 1 | 1.1, 2.4 | 0 | 6* | 1.2, 2.4 | 1.2 | 1.1 |

* The squared bias expression is minimized as $d \to \infty$.

## Appendix D

```
/************************************************************
*************************************************************
** This program compares designs based on the D-me criterion **
** to D-optimal designs for two-factor second order models.  **
**                                                           **
** The program produces results for one set of parameter     **
** values and a specific design situation.  In this example, **
** the vector of true coefficient values is                  **
** {beta0, beta1, beta2, beta12, beta11, beta22} =           **
** {1, 2, 1, 2, 1, 1}, and the initial design is a CCD with  **
** axial points at 2 and -2 and 3 center runs.               **
*************************************************************
************************************************************/


options nodate ls=80 formdlim='_';

/********************************************************* ***************
** Generating random numbers to use as seeds for the simulation data sets.  **
** Note: ndata should be large enough to complete the simulation following. **
****************************************************************************/

data random;
        ndata=140005;
        array randi{90}_temporary_;
        do i = 1 to ndata;
          if i = 1 then do j=1 to 90;
           randi{j} = ranuni(12);
          end;
          ran=ranuni(123);
          pos=int(ran*90) + 1;
          x = ran;
          ran = randi{pos};
          randi{pos} = x;
          output;
        end;
drop i j ran pos ndata;
run;

/******************************
** Starting the IML procedure **
******************************/

proc iml;

/**********************************************************************
** Creating the module: nsim is the number of simulated data sets in  **
** the simulation, fct is the standard deviation of the ME variable,  **
** ndata is the number of random numbers generated for the simulation,**
** and n is the number of design points in the initial design. Note:  **
** ndata should be the same value used in the preceding data step.    **
**********************************************************************/

start main(nsim,fct,ndata,n,ns);

   *declaring the covariance matrices;
     tvar=j(6,6,0); vtbeta=j(6,6,0);

/********************************************************************
** Creating the vector of random numbers from the data set "random" **
********************************************************************/

     use random;      read all into data;     data=1000*data;
```

```
/*******************************************
** Begin the do loop to simulate data sets **
*******************************************/

  do sim= 1 to nsim;

/************************************
** Generating the intial ME data set **
************************************/

      *specifying initial design;

         x={-2 0, 2 0, -1 -1, -1 1, 1 1, 1 -1, 0 -2, 0 2,0 0,0 0,0 0};

      *Creating model terms;

         int=x[,1]#x[,2];
         quad1 = x#x;
         ones = j(n,1,1); onep=ones`;

      *Creating model matrix;

         xm = ones||x||int||quad1; xmp= xm`; xpxinv=inv(xmp*xm);
         xp=x`;

      *Declaring the vectors needed to store simulation data;

         vsbeta=j(6,1,0);        svar=j(6,1,0);
         varb1=j(1,1,0);         varb11=j(1,1,0);
         varib1=j(1,1,0);         varib11=j(1,1,0);
         bshat=j(6,1,0);         bsihat=j(6,1,0);
         inf=j(6,1,0);         sfact=j(1,1,0);

      *Creating vectors of errors for y and ME variable;

         e = normal(data[1:ns+n,]);
         e1 = normal(data[ns+n+1:2*(n+ns),]);

      *Updating the vector of random numbers;

         data=data[2*(n+ns)+1:ndata,];
         ndata= ndata - (2*(n+ns));

      *Establishing parameters for the model;

         factor = fct;
         beta = 1//2//1//2//1//1;
         *Note: sigma=1 for the variance of y;

      *Creating the model matrix which includes ME to generate the data;

          u1=e1[1:n,]*factor;
          xme = x[,1] + u1||x[,2];
          intme=xme[,1]#x[,2];
          quad2 = xme#xme;
          xmem = ones||xme||intme||quad2;

      *Generating the data;

          y1 =xmem * beta + e[1:n,];

/***************************************************
** Computing OLS estimates of coefficients and MSE **
** as intial estimates for the IRWLS procedure.    **
***************************************************/

       *Computing variance of coefficients for OLS;
```

```
          bhat=xpxinv*xmp*y1;
          yhat=xm*bhat;
           mse=(onep*((y1- yhat)#(y1- yhat)))/(n-6);
          vcvb=xpxinv*mse;
          vb1=vcvb[2,2];          vb11=vcvb[5,5];

/**************************************
** IRWLS analysis of initial data set **
**************************************/

      *creating the new model matrix;

           sqfct=factor**2;
           ad1=j(n,1,sqfct);ad2=j(n,1,0);
           ad=ad1||ad2; quad3=quad1+ad;
           xm1 = ones||x||int||quad3; xmp1= xm1`;


      *computing variance of coefficients for IRWLS;

          constant=2*((factor**4))*bhat[5,1]**2;
         vary=(
               (mse#ones)
                +(((bhat[2,1])*ones + bhat[4,1]*x[,2]+ 2*(bhat[5,1])*(x[,1]))#
                    ((bhat[2,1])*ones + bhat[4,1]*x[,2]+ 2*(bhat[5,1])*(x[,1])))*(factor**2)
                +constant);
          vcvy=diag(vary);
          vinvy=inv(vcvy);
         msen=mse;
         varyn=vary;
         vcvyn=vcvy;
         vinvyn=vinvy;
          val=1;  k=1; cnt=j(1,1,1);
         yhati=yhat;
         thethat=bhat;

      *the interative procedure;

            do until (val < 10E-8);
              vcv=inv(xmp1*vinvyn*xm1);
              gamhat=vcv*xmp1*vinvyn*(y1-yhati);
              thethat=thethat+gamhat;
                th1=thethat[2,1];
                th11=thethat[5,1];
                th12=thethat[4,1];
             yhatn=xm*thethat;
              msen=(onep*((y1- yhatn)#(y1- yhatn)))/(n-6);
              const=2*((factor**4))*th11**2;
             varyn=(msen#ones +
                 ((th1*ones + th12*x[,2] + 2*th11*(x[,1]))
                   #(th1*ones + th12*x[,2] + 2*th11*(x[,1])))*(factor**2)+const);
             vcvyn=diag(varyn);
             vinvyn=inv(vcvyn);
              val=abs((onep*((y1- yhati)#(y1- yhati)))-((n-6)*msen));
             yhati=xm*thethat;
            k=k+1;
              if k=250 then val=-1;
              if k=250 then print k beta factor;
           end;

/**************************************************
** Creating the D-me optimal design, where optirw **
** is the optimal point for augmentation, and     **
** nirwls is the optimal determinant.             **
**************************************************/

*augmenting the n-point design with n more points;
```

```
j=1;
do j = 1 to ns;
   nirwls=0;
   optirw={5 5 5 5 5 5};

*checking the grid of candidate points;

   do newx1=-2 to 2 by .5;
   do newx2=-2 to 2 by .5;

     *the model term for the candidate point;

       quadx1=newx1*newx1;
       quadx2=newx2*newx2;
       newint=newx1*newx2;
        xo=1||newx1||newx2||newint||quadx1||quadx2;
       newxm=xm//xo; newxmp= newxm`;
       newones=newxm[,1];
       xcol=newxm[,2];
       quadcol=newxm[,3];

     *the covariance matrix for the data;

       const=2*((factor**4))*th11**2;
       varynew=(msen#newones
         +((th1*newones + th12*newxm[,3] + 2*th11*(xcol))
          #(th1*newones + th12*newxm[,3] + 2*th11*(xcol)))*(factor**2)+const);
       vcvynew=diag(varynew);
       vinvynew=inv(vcvynew);

     *the covariance matrix for the coefficients and its determinant;

       newxpxi=newxmp*vinvynew*newxm;
       dirwls=det(newxpxi);

     *comparing each candidate point to find the optimal;

       if (dirwls = nirwls) then do;
          optirw=optirw//xo;
      end;

       if (dirwls > nirwls) then do;
            optirw=xo;
            nirwls=dirwls;
      end;

   end;
   end;

    *the error values for y and x in the augmented data set;

       e2 = e[n+j,];
       e3 = e1[n+j,];

    *new data point;

        newxme= optirw[,2] + factor*e3;
        square=newxme*newxme;
        inte=optirw[,3]*newxme;
        y2= 1 + beta[2,]*newxme + beta[3,]*optirw[,3]
           + beta[4,]*inte + beta[5,]*square + beta[6,]*optirw[,6] + e2;
       y1=y1//y2;
        xm= xm//optirw; xmp=xm`;

    *the OLS estimates for the new data set;

        o=j(n+j,1,1);op=o`;
        xpxinv=inv(xmp*xm);
```

```
        bhato=xpxinv*xmp*y1;
        yhato=xm*bhato;
        mseo=(op*((y1- yhato)#(y1- yhato)))/(n+j-6);
        vcvbo=xpxinv*mseo;
        vb1o=vcvbo[2,2];
        vb11o=vcvbo[5,5];

    *creating augmented new model matrix for the IRWLS procedure;

        optirw[,5]=optirw[,5] + factor*factor;
        xm1 = xm1//optirw; xmp1= xm1`;
        x = x//optirw[,2:3];

    *computing covariance matrix of y for IRWLS procedure;

        constant=2*((factor**4))*bhato[5,1]**2;
        varyn=(mseo#o
             +((bhato[2,1]*o + bhato[4,1]*x[,2] + 2*bhato[5,1]*(x[,1]))
             #(bhato[2,1]*o + bhato[4,1]*x[,2] + 2*bhato[5,1]*(x[,1]))
               )*(factor**2)+const);
        vcvyn=diag(varyn);
        vinvyn=inv(vcvyn);
        msen=mseo;
        val=1;  k=1; cnt=j(1,1,1);
        yhati=yhato;
        thethat=bhato;

    *the iterative procedure;

        do until (val < 10E-8);
          vcv=inv(xmp1*vinvyn*xm1);
          gamhat=vcv*xmp1*vinvyn*(y1-yhati);
          thethat=thethat+gamhat;
            th1=thethat[2,1];
            th11=thethat[5,1];
            th12=thethat[4,1];
          yhatn=xm*thethat;
          msen=(op*((y1- yhatn)#(y1- yhatn)))/(n+j-6);
          const=2*((factor**4))*th11**2;
          varyn=(msen#o + ((th1*o + th12*x[,2] + 2*th11*(x[,1]))
              #(th1*o + th12*x[,2] + 2*th11*(x[,1]))))*(factor**2)+const);
          vcvyn=diag(varyn);
          vinvyn=inv(vcvyn);
          val=abs((op*((y1- yhati)#(y1- yhati)))-((n+j-6)*msen));
          yhati=xm*thethat;
          k=k+1;
          if k=250 then val=-1;
          if k=250 then print k beta factor;
        end;
*end of augmentation procedure;

  end;

*final calculation of coefficients for D-me Optimal design;

   quad=x#x;
   intne=x[,1]#x[,2];
   xme=x[,1]+ (factor*e1);
   qud=xme#xme;
   int=xme#x[,2];
   xmem=o||xme||x[,2]||int||qud||quad[,2];
   y1=xmem*beta + e;
   xmod=o||x||intne||quad; xmodp=xmod`;

*the OLS estimates for initial values in the IRWLS procedure;

   invxprx=inv(xmodp*xmod);
   bhat=invxprx*xmodp*y1;
```

```
    yhat=xmod*bhat;
    mse=(op*((y1 - yhat)#(y1 - yhat)))/(ns+n-6);

*the new model matrix for the IRWLS procedure;

    xmodadd=xmod[,5] + factor*factor#o;
    xmod1=xmod[,1:4]||xmodadd||xmod[,6];    xmod1p=xmod1`;
    cons=2*((factor**4))*bhat[5,1]**2;
    vary=(mse#o + ((bhat[2,1]*o + bhat[4,1]*x[,2] + 2*bhat[5,1]*(x[,1]))
    #(bhat[2,1]*o + bhat[4,1]*x[,2] + 2*bhat[5,1]*(x[,1]))))*(factor**2)+cons);
    vcvy=diag(vary);
    vinvy=inv(vcvy);
    val=1; k=1; cnt=j(1,1,1);
    yhati=yhat;
    thethat=bhat;

*the iterative procedure;

      do until (val < 10E-8);
         vcv=inv(xmod1p*vinvy*xmod1);
         gamhat=vcv*xmod1p*vinvy*(y1-yhati);
         thethat=thethat+gamhat;
           th1=thethat[2,1];
           th11=thethat[5,1];
           th12=thethat[4,1];
         yhatn=xmod*thethat;
         mse=(op*((y1- yhatn)#(y1- yhatn)))/(ns+n-6);
         const=2*((factor**4))*th11**2;
         vary=(mse#o + ((th1*o + th12*x[,2] + 2*th11*(x[,1]))
             #(th1*o + th12*x[,2] + 2*th11*(x[,1]))))*(factor**2)+const);
         vcvy=diag(vary);
         vinvy=inv(vcvy);
         val=abs((op*((y1- yhati)#(y1- yhati)))-((ns+n-6)*mse));
         yhati=xmod*thethat;
        k=k+1;
        if k=250 then val=-1;
        if k=250 then print k beta factor;
      end;

*calculation of covariance matrix and individual variances;

   vbeta=inv(xmod1p*vinvyn*xmod1);
   vi1=vbeta[2,2];
   vi11=vbeta[5,5];
   tconst=2*((factor**4))*beta[5,]**2;
   tvaryn=(o + ((beta[2,]*o + beta[4,]*x[,2] + 2*beta[5,]*(x[,1]))
                #(beta[2,]*o + beta[4,]*x[,2] + 2*beta[5,]*(x[,1]))))*(factor**2)+tconst);
   tvcvyn=diag(tvaryn);
   tvinvyn=inv(tvcvyn);
   vbeta=inv(xmod1p*tvinvyn*xmod1);

*storing IRWLS covariance matrix and coefficients and from the data set;

    vsbeta=vsbeta||vbeta;
    bsihat=bsihat||thethat;
    varib1=varib1||vi1;
    varib11=varib11||vi11;

/************************************************
** Computing IRWLS estimates based on the      **
** D-optimal design ignoring measurement error **
************************************************/

*the data;
   *x={-2 0, 2 0, -1 -1, -1 1, 1 1, 1 -1, 0 -2, 0 2,0 0,
      -2 -2, -2 -2, -2 -2, -2 2, -2 2, 2 -2, 2 -2, 2 2, 2 2};

   *x={-2  0,  2  0, -1  1, -1 -1,  1 -1,  1  1,
```

```
        0 -2,   0  2,   0  0,   0  0,   0  0,   2 -2,   2 -2,
        2 -2,  -2  2,  -2  2,  -2  2,  -2 -2,  -2 -2,  -2 -2,   2  2,   2  2};

     x={-2  0,   2  0,  -1  1,  -1 -1,   1 -1,   1  1,   0 -2,   0  2,
          0  0,   0  0,   0  0,   0 -2,   0  2,   2 -2,   2 -2,   2 -2,
          2 -2,   2  2,   2  2,   2  2,   2  2,  -2 -2,  -2 -2,  -2 -2,  -2 -2,
        -2  0,  -2  2,  -2  2,  -2  2,  -2  2};
    quad=x#x;
    intne=x[,1]#x[,2];
    xme=x[,1]+ (factor*e1);
    qud=xme#xme;
    int=xme#x[,2];
    xmem=o||xme||x[,2]||int||qud||quad[,2];
    olsy=xmem*beta + e;
    xmod=o||x||intne||quad; xmodp=xmod`;

*the OLS estimates for initial values in the IRWLS procedure;

    invxprx=inv(xmodp*xmod);
    bhat=invxprx*xmodp*olsy;
    yhat=xmod*bhat;
    mse=(op*((olsy - yhat)#(olsy - yhat)))/(ns+n-6);

*the new model matrix for the IRWLS procedure;

    xmodadd=xmod[,5] + factor*factor#o;
    xmod1=xmod[,1:4]||xmodadd||xmod[,6];    xmod1p=xmod1`;
    cons=2*((factor**4))*bhat[5,1]**2;
    vary=(mse#o + ((bhat[2,1]*o + bhat[4,1]*x[,2] + 2*bhat[5,1]*(x[,1]))
    #(bhat[2,1]*o + bhat[4,1]*x[,2] + 2*bhat[5,1]*(x[,1])))*(factor**2)+cons);
    vcvy=diag(vary);
    vinvy=inv(vcvy);
    val=1; k=1; cnt=j(1,1,1);
    yhati=yhat;
    thethat=bhat;

*the iterative procedure;

      do until (val < 10E-8);
         vcv=inv(xmod1p*vinvy*xmod1);
         gamhat=vcv*xmod1p*vinvy*(olsy-yhati);
         thethat=thethat+gamhat;
           th1=thethat[2,1];
           th11=thethat[5,1];
           th12=thethat[4,1];
         yhatn=xmod*thethat;
         mse=(op*((olsy- yhatn)#(olsy- yhatn)))/(ns+n-6);
         const=2*((factor**4))*th11**2;
         vary=(mse#o + ((th1*o + th12*x[,2] + 2*th11*(x[,1]))
             #(th1*o + th12*x[,2] + 2*th11*(x[,1])))*(factor**2)+const);
         vcvy=diag(vary);
         vinvy=inv(vcvy);
         val=abs((op*((olsy- yhati)#(olsy- yhati)))-((ns+n-6)*mse));
         yhati=xmod*thethat;
         k=k+1;
         if k=250 then val=-1;
         if k=250 then print k beta factor;
      end;

*the covariance matrix and coefficients of the D-optimal design;

     bhat=thethat;
     var=inv(xmod1p*vinvy*xmod1);
     vb1=var[2,2]; vb11=var[5,5];
     tconst=2*((factor**4))*beta[5,]**2;
     tvary=(o + ((beta[2,]*o + beta[4,]*x[,2] + 2*beta[5,]*(x[,1]))
            #(beta[2,]*o + beta[4,]*x[,2] + 2*beta[5,]*(x[,1])))*(factor**2)+tconst);
     tvcvy=diag(tvary);
```

```
     tvinvy=inv(tvcvy);
     var=inv(xmod1p*tvinvy*xmod1);

*storing OLS covariance matrix and coefficients;

    bshat=bshat||bhat;
    svar=svar||var;
    varb1=varb1||vb1;
    varb11=varb11||vb11;

*storing information from this data set;

    tvar=tvar+svar[,2:7];
    vtbeta=vtbeta+vsbeta[,2:7];
    b1that=b1that//bshat[2,];
    b11that=b11that//bshat[5,];
    b1tihat=b1tihat//bsihat[2,];
    b11tihat=b11tihat//bsihat[5,];
    vartb1=vartb1//varb1;
    vartb11=vartb11//varb11;
    varitb1=varitb1//varib1;
    varitb11=varitb11//varib11;


*end of the simulation;

end;

/*******************************************************
** Computing variance information for the simulated data **
** sets based on the coefficients and covariances of the **
** D and D-me design augmentation procedures.            **
*******************************************************/

   s=1/nsim; si=1/(nsim-1);
   add=j(1,nsim,s);
   ave=j(1,nsim,si);
   aveb1=add*b1that;
   ab1=repeat(aveb1,nsim,1);
   varb1=ave*((b1that-ab1)#(b1that-ab1));
   aveb11=add*b11that;
   ab11=repeat(aveb11,nsim,1);
   varb11=ave*((b11that-ab11)#(b11that-ab11));
   aveb1i=add*b1tihat;
   ab1i=repeat(aveb1i,nsim,1);
   varb1i=ave*((b1tihat-ab1i)#(b1tihat-ab1i));
   aveb11i=add*b11tihat;
   ab11i=repeat(aveb11i,nsim,1);
   varb11i=ave*((b11tihat-ab11i)#(b11tihat-ab11i));
   avevb1=add*vartb1;
   avevb11=add*vartb11;
   avevib1=add*varitb1;
   avevib11=add*varitb11;
   matave=s*tvar;
   matiave=s*vtbeta;
   detave=det(matave);
   detiave=det(matiave);
   deff=(detave/detiave)**(1/6);


   print fct beta;
   print deff detave detiave varb1 varb11 varb1i varb11i avevb1 avevb11 avevib1 avevib11;

*deff=the D-efficiency of the D-optimal design in relation to the Dme-optimal designs;
*detave=determinant of the average covariance matrix for the D-optimal design;
*detiave=determinant of the average covariance matrix for the Dme-optimal designs;
*varb1,varb11:variances of the simulated model coefficients from the D-optimal design;
*varb1i,varb11i:variances of the simulated model coefficients from the Dme-optimal design;
```

```
*avevb1,avevb11:average estimated variances of the model coefficients--D-optimal design;
*avevib1,avevib11: AEVs of the model coefficients--Dme-optimal design;

finish main;

run main(2000,.2,140005,11,19);
run main(2000,.4,140005,11,19);
run main(2000,.6,140005,11,19);
run main(2000,.8,140005,11,19);

*Note: module parameters are defined at the beginning of the IML procedure;

quit;
```

# Vita

## Angela Renee McMahan

I was born on April 29, 1969, the daughter of Dennis W. and Brenda F. McMahan. I grew up in Knoxville, Tennessee, and graduated as valedictorian from Halls High School in 1987. I received a National Merit Scholarship and a Wiley Mathematics Scholarship to attend Furman University in Greenville, South Carolina. In 1991, I earned a Bachelor of Science in Mathematics from Furman, graduating Summa Cum Laude. I was awarded the Delaney Medal in Mathematics for the highest grade point average among Mathematics majors. I entered the graduate program in Statistics at Virginia Polytechnic Institute and State University in the fall of 1992 and completed requirements for a Master of Science degree in Statistics in the Spring of 1994. During the summer of 1996, I interned at Intel Corporation in Albuquerque, New Mexico. I received a P.E.O. Scholar Award for my last year of Ph.D. study. In April of 1997, I completed the requirements for a Doctor of Philosophy degree in Statistics from Virginia Polytechnic Institute and State University.